A.M.A.
Archives OF OPHTHALMOLOGY

MAY 1956

VOLUME 55 NUMBER 5

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Experimental Studies of the Choroidal Vessels
Enrique Wudka and Irving H. Leopold

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J. V. D. Quereau and B. F. Souders

Diseases of the Retina and Optic Nerve
Henry P. Wagener

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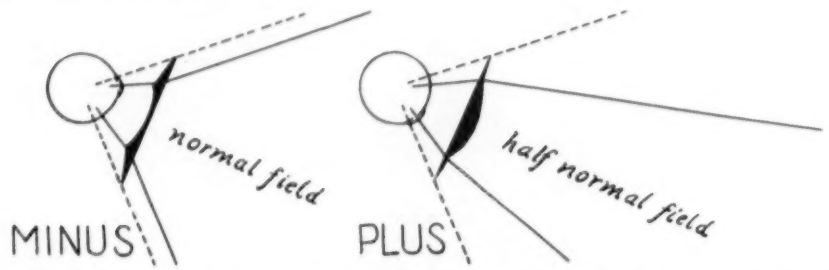

From these basic facts, the conclusion is obvious that due to the increased field of vision in minus lenses, the use of lenticular form is desirable. However, in strong plus lenses—particularly cataract lenses—due to the restricted field of vision the lenticular form is not advised.

Our next Scientific Corner article will discuss the various types of cataract lenses —their advantages and disadvantages.

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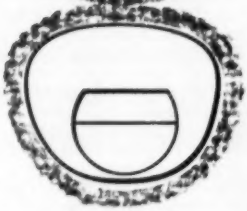

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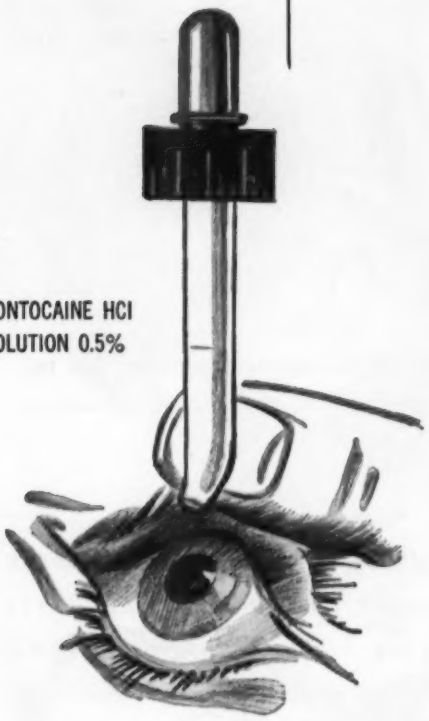

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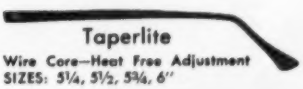

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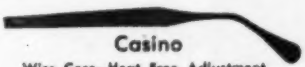

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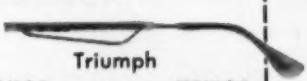

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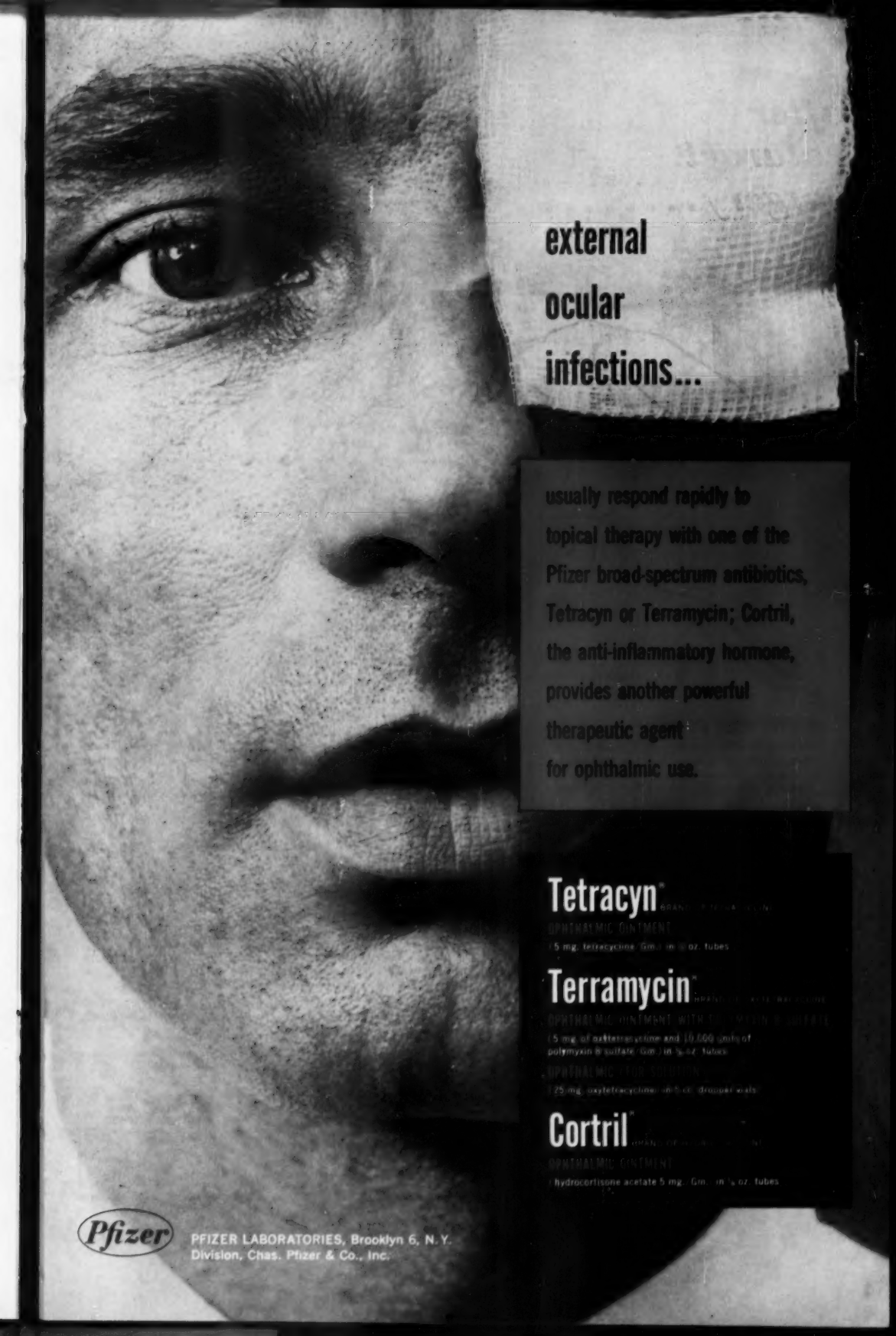
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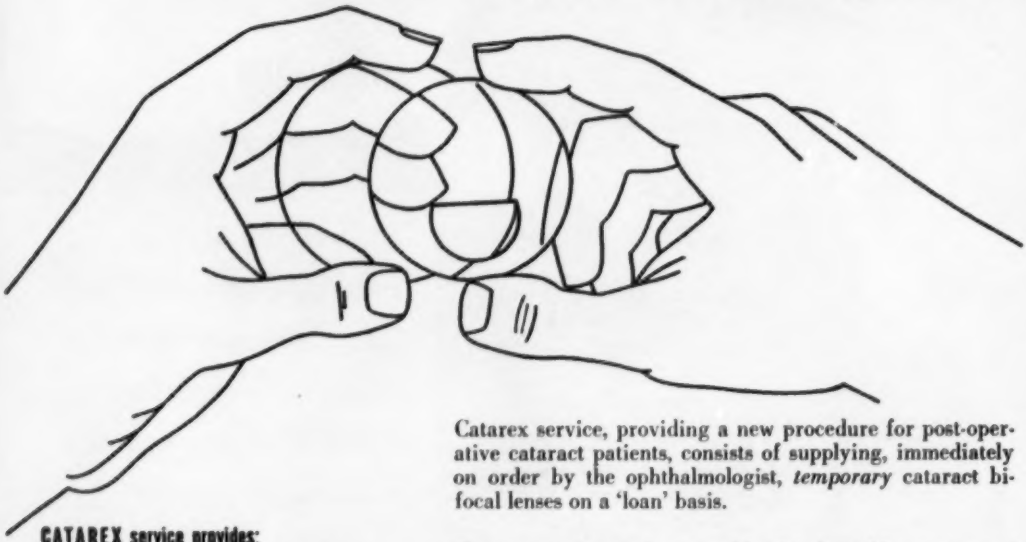

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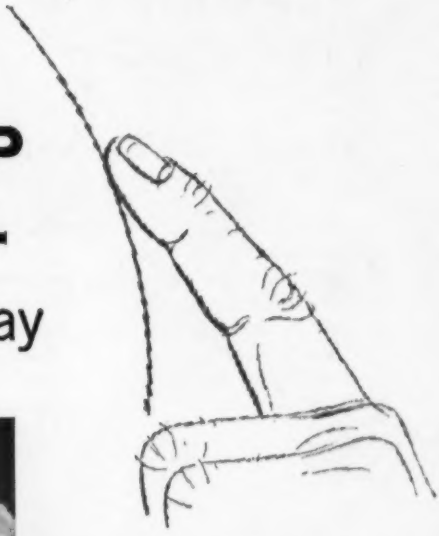

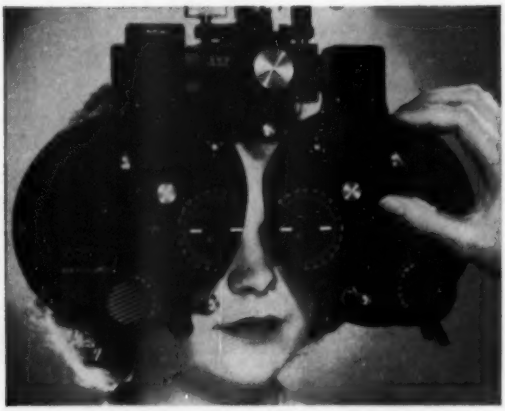

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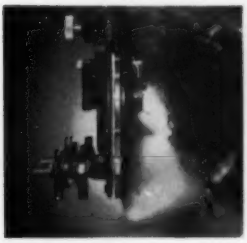

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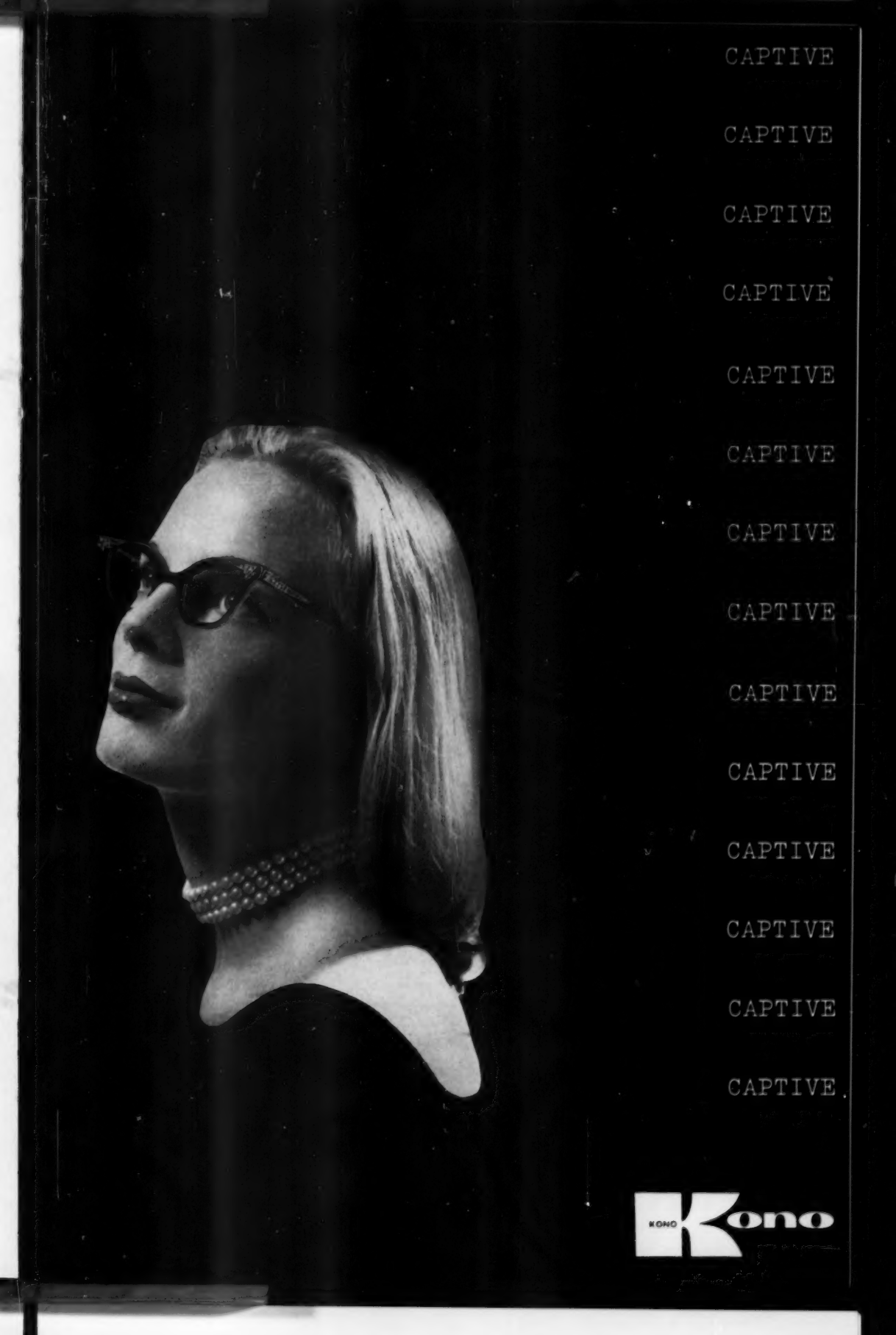
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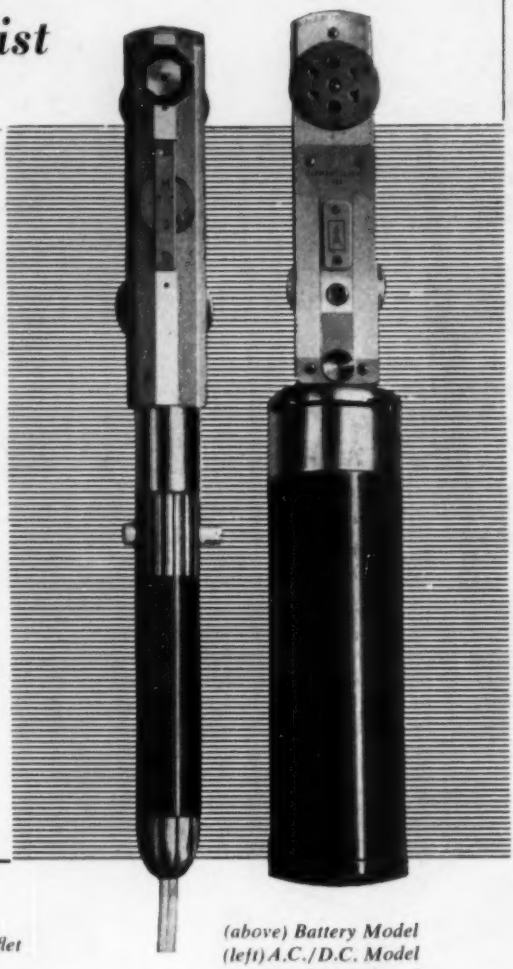

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Concurrence of Macular Edema with Cataract Extraction

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Montreal, Canada

By its very nature, macular edema must be a common occurrence after cataract extraction, and yet little reference to it can be found in the literature. I have canvassed several ophthalmologists for their experiences. Among my confreres in Montreal, none * had been aware of it before my original paper, in 1954.[1] Kirby † stated that he had "seen it frequently after glaucoma surgery but not after cataract operation." He felt that it is likely to follow any opening of the eye. Stallard ‡ stated that he had had two cases. Chandler § believes that he has had several cases and that the patient usually gets well spontaneously. Since my report in 1954 sporadic cases have been reported to me.

As a disease entity, of course, macular edema is very common and is well known. It has been studied by many. Aside from those cases of inflammatory origin, the majority of workers believe the condition is due to a "disturbance in circulation." As the lesion is so well known, I wish to do no more than review the highlights. The circulation in the macular region is particularly vulnerable. Some explanation for this may be deduced from histologic study. The nutrition of the macula, obtained by way of the choroid, is at least as ample as that of the rest of the retina. But, as Duke-Elder [2] and many others have pointed out, the retinal tissue of the fovea and immediate vicinity is entirely avascular. In the surrounding area are numerous capillaries supplied by arterioles quite some distance away. Coupled with this scanty blood supply, the nutritional requirements are relatively great, owing to the density of the neuronal elements.

Thus, it is obvious that the nutritional reserve in this area must be relatively small, and that any reduction in the minute volume of the blood flow will have a severer effect here than in other parts of the retina. I believe the circulatory disturbance is a slowing of the capillary flow brought about by narrowing of the

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From the Department of Ophthalmology of the Royal Victoria Hospital and McGill University.

* MacMillan, J. A.: Personal communication. Ramsey, G. S.: Personal communication.

† Kirby, D. B.: Personal communication.

‡ Stallard, H. B.: Personal communication.

§ Chandler, P. A.: Personal communication.

arterioles, owing either to sclerosis or to spasm or to a combination of the two conditions. This dysfunction may occur primarily in the retinal circulation or in the choroidal circulation or in both. This view is not original with me. It has been put forth by many others—Horniker,[3] Duke-Elder,[4] Bailliart,|| Duggan,[7] Berens,[8] Benedict and Wagener,[9] and Klien.[10] In 1952 I [11] described a series of cases which exemplified different types of macular edema in which there was no cataract, in an attempt to show that these cases formed an interrelated group and to demonstrate clinically this picture, described by so many others. I attempted to show that many of these patients suffer from anxiety, and that this frequently is the precipitating cause. This opinion is supported by Horniker,[3] Harrington,¶ and Zeligs.[14] It was my experience that when the anxiety was controlled and the patient was given vasodilators, improvement often occurred.

I wish now to present the salient features of nine cases (eight patients) of this condition occurring in association with cataract extraction. These cases have come under my care since 1949. Seven of them were reported in some detail in 1954.[1] I shall review them briefly, adding the details of some later occurrences, which, I believe, help to explain matters. To the original seven cases I shall add two new ones.

REPORT OF CASES

Case 1.—The patient first came under my care in September, 1946, at the age of 82. She had early nuclear cataracts, permitting 6/20 vision (corrected) in each eye. Save for a blood pressure of 180/90 mm. Hg, her general health was excellent. A detailed view of the fundi could not be obtained.

On Dec. 1, 1949, an intracapsular cataract extraction with round pupil and two peripheral iridectomies was carried out successfully on the right eye. At the time of operation the patient was somewhat nervous and tense but not markedly so. Except for a small hyphema on the fifth day, which rapidly disappeared, convalescence was uneventful.

At examination 50 days after operation the eye appeared perfectly normal and quiet. The fundus, except for mild arteriolar sclerosis, was quite normal. The pupil was round, and the vitreous face was intact. With +12.50 D. sph she read 6/7 partly. There was no astigmatism. The patient reappeared for a check 107 days after operation, stating that the vision of the right eye had been slightly blurred and the pupil deformed for about a week. Examination showed the latter to be a horizontal oval. A tongue of vitreous had prolapsed through the pupil and was adherent to the operative wound above. The vision was 6/12 with her best correction, and her fundus, except for the arteriolar sclerosis, appeared normal. When examined 10 days later, the vision of the right eye was poorer, being 6/18. The pupil was unchanged. On this occasion the macula was mildly edematous and showed pigment mottling. There were no hemorrhages or exudates. The patient was placed on physostigmine drops. Ten days later, i. e., 127 days after operation, the pupil was rounder and the fundus quite normal. The vision was 6/7 partly. Two weeks later the condition was further improved. The pupil was quite round and the vision 6/6 partly. The vitreous was completely behind the pupil.

The patient has been seen at intervals since that time. The eye remained quite normal until the spring of 1954. At this time the macula became edematous again and the vision fell to 6/12 partly. Nicotinic acid 50 mg., t. i. d., a. c., was prescribed. Within five or six weeks the vision returned to the previous level. At this time the nicotinic acid was stopped. There was a recurrence in October, 1955. At this time the nicotinic acid was restarted, and the condition again improved. On neither recurrence did the vitreous prolapse again. An interesting point is that with each recurrence there was an increase in the hyperopic correction by 1 to 1.5 D.

Case 2.—The patient first came under my care in 1947 with nuclear cataracts, at the age of 70. The patient was high-strung, excitable, and emotionally unstable, though not neurotic. He had rather marked hypertension—240/100 mm. Hg. In all other respects he was apparently

|| References 5 and 6.

¶ References 12 and 13.

healthy. The fundus details could not be seen. On Oct. 3, 1949, an intracapsular cataract extraction with round pupil and two peripheral iridectomies was carried out. The patient made an uneventful recovery.

When he was examined 45 days later, the eye was fairly quiet, and the pupil was round, though very slightly displaced to the nasal side. The vitreous face was intact. The fundus showed only mild generalized arteriolar narrowing and sclerosis. There were no hemorrhages or exudates, and the macula and nerve head were normal. With +12.00 D. sph⁀+0.75 D. cyl, x 160, he read 6/9 partly. The patient was rechecked a week later and the eye was found unchanged.

The patient returned 105 days after operation, saying that his vision had been blurred for several days and the pupil deformed. The nasal half of the pupil was found to be retroverted. A prolapse of the vitreous through the pupil was adherent to the nasal half of the operative wound. The fundus appeared as described above; no macular disturbance was noted. Vision was 6/18. The patient was placed on treatment with physostigmine drops, with no improvement in the pupil. A month later the vision had improved to 6/15 partly. By this time it was felt there was macular edema. During the next several weeks the vision gradually improved to 6/9. However, there was no change in the pupil or in the prolapsed vitreous.

Since the spring of 1950 the patient has had several recurrences of macular edema in the right eye. The vision has fluctuated between 6/9 and 6/20. With each visual loss an increase in photophobia and macular edema occurred. Each attack was treated first with nicotinic acid 50 mg., t. i. d., a. c., and later with tolazoline (Priscoline) hydrochloride 25 mg. t. i. d., a. c. Throughout this time there has been no evidences of pigmentary change or degeneration. The vitreous face has remained unchanged. With each attack there has been a temporary mild increase of the hyperopia.

In the spring of 1953 the patient had a rather severe coronary occlusion. Following this he had recurrent angina pectoris, which culminated in a fatal occlusion in June, 1955. Unfortunately, as the patient died many miles from Montreal, it was impossible to obtain his eye for examination.

Case 3.—The patient first came under my care in March, 1950, for cataracts, at the age of 75. The fundi could not be examined. The patient was apparently healthy except for moderate hypertension. The blood pressure was 200/95 mm. Hg at admission but decreased slightly later. The patient was very unstable emotionally, being excitable and dependent. Because of her long convalescence, owing to complications, her emotional status became even more unstable.

On Aug. 20, 1951, an intracapsular cataract extraction with round pupil and two peripheral iridectomies was attempted. At operation the patient lost her nerve. At the moment the lens capsule was grasped, she sat up. Thus, the lens was subluxated below and had to be removed with a loop, after a full iridectomy. There was little loss of vitreous. The wound was closed with the preplaced corneal sutures. Two days after operation, during a nightmare, the patient became disorientated, with resulting prolapse of the iris. She was taken to the operating room, and this was excised. There was a small hyphema at this time.

The eye healed well. The pupil was only slightly hammock-shaped. The vitreous remained adherent to the corneoscleral wound above. The vision slowly improved and the vitreous cleared, so that 100 days after operation with +9.50 D. sph⁀+1.00 D. cyl, x 180 the vision was 6/9 partly. The fundus appeared normal save for mild arteriolar sclerosis.

The patient returned 197 days after operation, stating that the vision in the eye operated on appeared "fluttery" and that there was a central blind spot. Examination showed the vision to be 6/18 partly. The macular area was quite edematous; a small pale area was present in the center that had the appearance of a cyst. Slit-lamp examination showed a posterior vitreous detachment but no appreciable vitreous degeneration.

The patient was placed on nicotinic acid 50 mg., t. i. d., a. c., and some weeks later on tolazoline 25 mg., t. i. d., a. c. The latter had to be discontinued because of intolerance, and the patient returned to nicotinic acid. In four to six weeks the vision improved to 6/7 and the edema of the macular area subsided, leaving a very fine pigment mottling. The apparent cyst disappeared.

The eye remained quiet with no change for about a year. Then in March, 1952, the patient had another bout of macular edema, which very slowly improved. By August the vision had recovered to 6/7. There was a further exacerbation in May, 1953, which improved only 10 months later, with her vision restored to 6/12 partly. Since that time the patient has had no recurrences. There has been no further change of the vitreous. Each recurrence was marked by a slight increase in the hyperopia.

Case 4.—The patient first came under my care in 1948 for refraction, at the age of 60. Within three years he began to develop cataracts, requiring operation on the right eye on June

16, 1954. The patient's health was good save for a history of gout and mild hypertension. The blood pressure was 170/105 and dropped only slightly within a few days after admission. An intracapsular cataract extraction with round pupil and two peripheral iridotomies was carried out. The wound was closed with one preplaced mattress-type absorbable surgical suture. At the first dressing, next day, it was found that the wound was gaping slightly at 12 o'clock, under the conjunctival flap, owing to parting of the corneoscleral sutures. Next day the pupil was pulled up slightly in this region. On July 3 a prolapse of vitreous adherent to the wound was noted. In the period immediately following operation the patient developed an attack of gout, which rapidly came under control with colchicum. During the whole convalescent period the patient was nervous and apprehensive.

Vision in the eye operated on was slow to recover, owing to a corneal haze. Fifty-five days after operation it was 6/18. On this occasion there was a small central scotoma, and, though the fundus could be seen clearly, the fovea was hazy. The patient was put on tolazoline 12.5 mg., t. i. d., p. c., the dose being gradually worked up to 25 mg., t. i. d., p. c. Within two weeks the vision had improved to 6/9 partly. At the examination 104 days after operation the vision had improved to 6/7. Further slow improvement occurred over the next three or four months. The eye retained a high degree of astigmatism, the final correction being +8.50 D. sph⁀6.00 D. cyl, x 175=6/6. There have been no recurrences.

Case 5.—The patient first came under my care for nuclear cataracts in October, 1948, at the age of 62. She was a nervous, high-strung person. Her general health was good; her blood pressure was 130/90. At one time the patient was thought to have pernicious anemia. However, careful investigation ruled this out. Fundus examination could not be carried out because of the lenticular opacities. On Oct. 17, 1951, an intracapsular cataract extraction with round pupil and two peripheral iridectomies was carried out on the right eye. The patient made an uneventful recovery. On the 50th day after operation the vision in the right eye with +11.00 D. sph⁀ D. cyl, x 170 was 6/18 partly. Ophthalmoscopy disclosed very mild generalized arteriolar narrowing and sclerosis. There was a small patch of waxy exudate just above the foveal region but no other exudates or hemorrhages. The foveal region was slightly hazy, and no pit could be discerned. There was no pigmentary disturbance. The patient was placed on tolazoline 25 mg., t. i. d., p. c. She did not tolerate this medication well but persisted with it. Ninety-three days after operation the vision had improved to 6/6 partly, and on this occasion the waxy exudate and the edema of the fovea had disappeared.

On Nov. 24, 1952, an extracapsular extraction with round pupil and two peripheral iridectomies was carried out on the left eye. On this occasion her blood pressure was 175/95 mm. Hg but fell slightly during the next few days in hospital. It is a question whether or not this patient should be considered hypertensive. Certainly, she had labile blood pressure and must be considered prehypertensive at least.

Twenty-five days after operation the vision of the left eye was correctible to 6/9. On Jan. 21, or 58 days after operation, the vision in the left eye with correction had fallen to 6/12. The macular area in the left eye now showed slight edema and was flecked with minute pale-yellow punctate spots. There was no change in the fundus of the right eye, and its vision remained at 6/6. This time the patient was given no medication. By April 21, or 122 days after operation, vision in the left eye had improved to 6/6 with +11.25 D. sph⁀+1.00 D. cyl, x 140. At all times the vitreous face remained intact in both eyes.

This patient has been followed carefully since operation. Gradually the whole of both fundi has become more tessellated. Minute punctate yellowish-white spots, apparently drusen, have appeared in both macular regions, but there is no edema. The patient has had several periods of emotional stress since 1952. Her husband for years has been troubled with glaucoma and has had several acute attacks in a blind eye which have been very difficult to control. On each occasion the patient has been greatly upset. In October, 1955, she was operated on for suspected carcinoma of the cecum. The patient, who is a graduate nurse, is aware of the possibilities. During all these stresses there has been no recurrence of her eye trouble.

Case 6.—The patient first came under my care in December, 1951, for early cataracts at the age of 61 years. The fundi were essentially normal. Save for mild arteriosclerosis, the health was excellent. The blood pressure was 140/80. An intracapsular extraction with round pupil and two peripheral iridotomies was carried out on the left eye on Feb. 21, 1955. The patient made an uneventful recovery. Thirty-six days following operation vision in the right eye was 6/7 with a correction of +8.50 D. sph⁀+3.00 D. cyl, x 180. The pupil was round and regular,

and the vitreous face was intact. The patient complained, however, that the vision of the right eye blurred periodically. This was particularly noticeable in my office, where, while carrying out refraction, the vision would gradually fail and then recover after a rest. It was difficult to carry out accurate refraction, as the hyperopia fluctuated. It was noted that the macula was mildly edematous, but there were no pigmentary changes and no hemorrhages or exudates. The retinae showed very mild arteriolar sclerosis, but the arterioles were of normal caliber. No medication was prescribed, and the patient's symptoms gradually subsided, disappearing during the next 21 days. Vision in this eye has remained at 6/6 partly since, with no recurrence of his trouble. At all times the vitreous face has been intact.

CASE 7.—The patient first came under my care in February, 1952, for nuclear cataracts at the age of 81. He was a relatively healthy man, but of nervous disposition. He recently had lost his wife. This, with his failing vision, had caused him considerable anxiety, and he approached operation with great emotional stress. His blood pressure was 170/78 mm. Hg. Except for marked generalized arteriosclerosis, his general health was good.

On March 31, 1952, an intracapsular cataract extraction with round pupil and a single peripheral iridectomy was carried out. Save for a small hyphema, which developed on the fifth day after operation, his recovery was uneventful. This hyphema took a long time to absorb. Only on the 63d postoperative day did it clear sufficiently for the fundus to be seen. There was moderate arteriolar sclerosis, and the macula was hazy and stippled with pigment. With +11.00 D. sph⌒+2.00 D. cyl, x 10 the vision was 6/18. The patient was placed on tolazoline 25 mg., t. i. d., a. c. Three weeks later the vision improved to 6/12. But a small central scotoma persisted. Following this the vision remained stationary for several months, but then gradually began to decrease in spite of all treatment, so that at the end of a year it was 6/240. There has been no further change. At all times the vitreous face has remained intact.

CASE 8.—The patient first came under my care for cataract of the left eye with complicating myopia at the age of 79. Previously a cataract had been removed successfully from the right eye by the late Dr. J. A. MacMillan. In this eye, with +1.00 D. sph⌒+1.00 D. cyl, x 15 the vision was 6/6. There was a large area of myopic degeneration which extended from the nerve head halfway to the fovea. The fovea appeared to be intact, however. There was mild generalized arteriolar sclerosis.

The left eye was myopic also, but the fundus could not be seen, owing to a nuclear cataract. The general health and temperament were excellent. The blood pressure was 110/70. On May 12, 1952, an intracapsular cataract extraction with round pupil and a single peripheral iridectomy was carried out. She was discharged from hospital after an uneventful convalescence. There was a small retroversion of the pupil at 12 o'clock, but the vitreous face was intact. The fundus could be seen well. There were a large myopic crescent and a large area of myopic degeneration extending from the disc almost to the fovea. The foveal pit could not be seen. There were no hemorrhages or exudates. Thirty-seven days after operation the left eye was quiet, and its vision with +2.00 D. sph, x 180 was only 6/120. On this occasion it was seen that the foveal region was edematous. The patient was placed on nicotinic acid 50 mg., t. i. d., a. c. She did not tolerate tolazoline. By Oct. 20, i. e., 161 days after operation, the vision of the left eye had improved to 6/30, and there were definite metamorphosia and central scotoma. The edema of the foveal region had decreased. Sixty days later the macular edema was still present, and a small patch of pigment just up and in from the fovea could be seen. The vision was 6/20. Thirty days later the vision was 6/18 and has remained at this level since, with no recurrence. The right eye has remained unaffected at all times. The vitreous face in each eye has remained intact.

COMMENT

It will be seen from the Table that there is more than one possible cause of the macular edema in most of these patients. I shall deal first with Cases 5, 6, 7, and 8, as they seem most straightforward and therefore can be disposed of most easily.

As already pointed out, I believe that macular edema per se in many cases is of vascular origin.# The disturbance, in my opinion, is due to slowing of the capillary flow, brought about by either arteriolar sclerosis or arteriospasm or a combination of the two. There is considerable evidence that anxiety is the precipitating factor

References 1 and 11.

Essential Characteristics of Patients Suffering from Macular Edema Following Cataract Extraction

Case No.	Age at Operation	Sex	Blood Pressure	Preoperative Complications	Operative Complications	Postoperative Complications	Date of Appearance, Days	Onset of Macular Edema	Follow-Up	Final Vision	Possible Etiology
1	86	F	180/90	Arteriolar sclerosis; hypertension	Nil	Hyphema; prolapse vitreous	5 100	100 days possible; 117 days certain	6 yr.: recurrence of macular edema	6/6 pt. to 6/9 pt.	Arteriolar sclerosis; cataract extraction with vitreous prolapse
2	72	M	240/100	Arteriolar sclerosis; hypertension	Nil	Prolapse vitreous	100	100 days possible; 135 days certain	6 yr.: recurrence of macular edema	6/9 to 6/20	Arteriolar sclerosis; anxiety; cataract extraction with vitreous prolapse
3	76	F	200/95	Arteriolar sclerosis; hypertension	Vitreous lost	Prolapse iris; hyphema	2 2	197 days	4½ yr.: recurrence of macular edema	6/7 to 6/12	Arteriolar sclerosis; anxiety; complicated cataract extraction with prolapse of vitreous
4	66	M	170/105	Arteriolar sclerosis; gout; hypertension	Nil	Rupture wound; prolapse vitreous	1 2 (possible)	Unknown; 55 days certain	20 mo.: no recurrence	6/6	Arteriolar sclerosis; anxiety; rupture of wound with prolapse of vitreous
5 OD	65	F	130/90	Nil	Nil	Nil	..	Unknown	4½ yr.: no recurrence	6/6	Anxiety; vasospasm; cataract extraction
OS	66	F	175/95	Nil	Nil	Nil	..	58 days	3½ yr.: no recurrence	6/6	Same
6	65	M	140/80	Arteriolar sclerosis (mild)	Nil	Nil	..	36 days	18 mo.: no recurrence	6/6	Arteriolar sclerosis; anxiety(?); cataract extraction
7	81	M	170/78	Arteriolar sclerosis (marked)	Nil	Hyphema	5	Unknown	4 yr.: slow loss to 6/240	6/12 to 6/240	Arteriolar sclerosis; anxiety; cataract extraction
8	79	F	110/70	Arteriolar sclerosis; myopia	Nil	Nil	..	Unknown; 37 days (?)	4 yr.: no recurrence	6/18	Arteriolar sclerosis; cataract extraction; myopia

in many cases; particularly is this so in central angiospastic retinopathy. The left eye of Patient 5 showed a typical example of the last condition. The disturbance in the right eye was not so typical, but I believe it should be included in the same group. Though anxiety was a marked feature in this case, I do not believe that it was the only precipitating factor. If this had been true, why did she not have recurrences recently, during the serious illnesses of herself and her husband? I was attending the patient for her eyes on both these occasions and can vouch for the fact that she was greatly disturbed. However, there was no recurrence in either eye. One is forced to assume, therefore, that a second factor was operating, and this probably was her cataract extraction.

I believe that Case 6 is a very mild example of the same combination of circumstances. Patient 7 had a typical case of so-called senile macular degeneration. I do not believe that his cataract extraction precipitated his trouble. He was an old man with advanced arteriosclerosis, and I believe that the latter was the main cause. It is possible that a mild degree of superimposed angiospasm relative to his anxiety at the time of operation, and to the operative trauma, may have aggravated matters. In Patient 8 there was no emotional disturbance, but there was a high degree of myopia with secondary retinal degeneration. I believe in many cases that myopic degeneration also may be explained best on a vascular basis, in that enlargement of the posterior segment of the sclera produces relative ischemia. Further, this patient also had a mild arteriolar sclerosis. In my opinion, the operative trauma, affecting an area having a critical blood supply, precipitated the edema. The apparent response to vasodilatation, while definite, was slow, and recovery was not complete.

Slit-lamp examination of the posterior vitreous showed no disturbance in Patients 5 and 7. In Patients 6 and 8 there were a slight detachment of posterior vitreous and some mild vitreous degeneration. With the exception of Patient 8 and the left eye in Patient 5, this examination, unfortunately, was possible only some time after operation.

The first four cases are the most interesting, as they give rise to so many interesting speculations. The first three launched me on this study. There are a number of common features among these patients. They all had varying degrees of hypertension, suggesting an unstable peripheral circulation. In all there was a prolapse of the anterior vitreous. In the first two patients this occurred sometime after operation, apparently at the same time as the macular edema. The exact time relation in these two patients was impossible to determine. In the fourth patient the prolapse of the vitreous occurred almost immediately after operation, and probably at the same time the wound broke down. The second, third, and fourth patients were anxious and agitated during the whole operative period. In the first patient these features, while present, were not severe. In all four patients there was a separation of the posterior vitreous with no degeneration. Unfortunately, I was unable to determine the exact moment at which this vitreous detachment occurred.

I believe that in these four patients, also, vascular dysfunction was the underlying cause of the macular edema. All four patients had hypertension. Possibly the cataract extraction disturbed the local circulation further. Anxiety also may have been a factor in some cases. Indeed, in Patient 3 it may have been the main or only one. Certainly, she was in a most disturbed state for a long time. Possibly the vitreous prolapse was a causative factor in other cases.

In these four patients one cannot help speculating on the relationship of the vitreous prolapse to the occurrence of the macular edema. In Patient 3 the prolapse occurred at the time of operation, whereas the macular edema occurred more than five months later. In Patients 1 and 2 they occurred at about the same time, and probably also did so in Patient 4.

Which was the cause and which was the effect? The prolapse possibly could have played either role. In the first two cases, since there was no evidence of damage to the vitreous immediately after operation, and since there was no evidence of trauma postoperatively, possibly the vitreous prolapse was the effect and not the cause. Perhaps the sequence of events was this: macular edema with a collection of a preretinal transudate, which resulted in the separation of the vitreous and in its being forced forward, causing the anterior hyaloid membrane to break at some weak point.

Harrington,[15] in 1952, gave an excellent description of the changes in the vitreous face following cataract extraction. He has shown that the vitreous face undergoes great change in even so-called normal patients. More recently, Holland [16] has shown how frequent is disturbance of the vitreous face after cataract extraction. It is possible in the present patients that some distortion or traction was produced in the anterior vitreous by the healing process, such that some slight, unnoticed trauma caused a break in the hyaloid membrane, permitting the vitreous to pass forward into the anterior chamber. Possibly this prolapse permitted a separation of the posterior vitreous, and this last event was the precipitating factor in the production of the macular edema.

At first, this latter theory seemed to be the most acceptable. It still is most attractive. I find it difficult to believe that a transudate developing preretinally can produce sufficient pressure to push the vitreous forward. However, the subsequent behavior of Patients 1 and 2 indicates that some variation of this theory may approach the truth. Possibly the forward movement of the vitreous may be accounted for on the basis not only of a transudate into the preretinal space but also of engorgement and swelling of the choroid, this same swelling and engorgement, of course, being the cause of the transudate. In both these patients it is interesting to note that with the recurrences of their macular edema, their hyperopic correction increased by 1.00 to 1.50 D. In Patient 6 the process could be followed in the office. In this manner, then, the vitreous may have been pressed forward, and this, in the presence of a distorted vitreous face, may have caused rupture of the hyaloid membrane and a prolapse of the vitreous into the anterior chamber. Separation of the posterior vitreous has persisted in all four patients. This may be accounted for possibly by a recurrence of the preretinal transudate, but also there may be vitreous shrinkage secondary to vascular disturbance of the retina and choroid.

I have discussed these cases with many of my confreres. It has been suggested that the macular edema may have been purely of traumatic origin, occurring as a result either of operative injury or of a postoperative blow, being of the nature of a commotio retinae. All these patients were questioned carefully regarding the possibility of injury. They all are responsible persons, and I feel they must be believed when they say they know of no such injury. Injury at the time of operation cannot be ruled out, but it certainly could not have been the cause in the first three patients, in whom the onset of macular edema was long after operation. Stallard *

* Stallard, H. B.: Personal communication.

and Chandler † both have suggested that postoperative iritis may have been the cause. All these patients were followed closely, and at no time was there any evidence of uveitis. Chandler † has noted, however, that his cases occurred most frequently among patients with a stormy postoperative course. He favors the view that the vitreous changes are the prime and precipitating factors. The possible involvement of the vitreous calls to mind the vitreous syndrome described by Irvine [17] in 1953. In this condition, after cataract extraction, the vitreous sometimes shrinks and then prolapses forward, becoming adherent to the wound. Associated with this, recurrent spells of irritability and macular degeneration develop in the eye. Apparently, all gradations in severity of the syndrome may occur. My first two patients, and possibly the fourth, fit in this category very well, though the irritability feature was absent and the vitreous shrinkage and macular degeneration were not particularly marked. Irvine's paper is a most painstaking study of this syndrome. He apparently believes that vitreous shrinkage is the basic factor. However, to me it seems impossible for the vitreous to initiate changes by itself. To me, the vitreous changes must always be secondary. The vitreous is dependent upon the surrounding structures for its nutrition. So, while accepting Irvine's findings, I feel one must add vascular dysfunction as a causative factor.

What part may be played by the hypotony that occurs after cataract surgery? This phenomenon recently has been studied and reported by Hilding.[18] It may well play a part. But, because of the time relation, I feel it must be a minor one.

In all probability in some cases, as in my first two, it is impossible to determine what is cause and what is effect, as all factors are so closely related. In the present study the most important point of all, and the one which has the most practical significance, is that recovery was relatively good in all but one patient. Chandler † has also emphasized this point. It is impossible to assess fully the value of vasodilating drugs. Patients 1 and 2 in their first attacks, Patient 5 with her left eye, and Patient 6, all recovered without the use of vasodilators, suggesting that such drugs have little value. Chandler † is fully in accord with this view. However, these drugs do no harm; and, by analogy with the results from their use in patients with macular edema not associated with cataract extraction, I believe they may be of some value, and therefore should be given at least a trial.

SUMMARY AND CONCLUSIONS

Nine cases, in eight patients, of macular edema in association with cataract extraction are presented.

In five cases, the disturbance definitely occurred quite some time after operation.

In four cases, the disturbance probably occurred at about the time of operation.

In four cases, the disturbance was associated with prolapse of the vitreous forward.

It is suggested that the predisposing cause is a vascular instability in the retina and/or choroid in the macular region, partly at least brought about by cataract extraction. Five of these patients had vascular hypertension to some degree.

It is suggested that the precipitating cause in some cases was anxiety, possibly producing vasospasm, while in others prolapse of the vitreous through the pupil played a part.

† Chandler, P. A.: Personal communication.

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Experimental Studies of the Choroidal Vessels

I. Historical Survey
II. Methods and Material of Investigation
III. Anatomical Observations

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I. HISTORICAL SURVEY

The present name of the choroid is derived from the Greek: χόριον, membrane, and εἶδος, form, alluding to its vascular character, resembling that of the chorionic membrane, which envelops the fetus in the uterus. In this connection, it is interesting to note that the comparison established in the etymological derivation emphasizes the early recognition of the essential nature of this portion of the uveal tract. The fact that the main mass of the choroid is formed by vessels was also at a later period implied by Casserius and von Haller, who, respectively, called it the membrana sanguinolenta oculi and membrana vasculosa oculi.[1]

Rufus the Ephesian [2] applied the term "chorion-like tunic" to that portion of the uvea which lines the sclera inwardly. Galen the Pergamenian [3] regarded the middle coat of the eye as a continuation of the pia mater through the vascular investment of the optic nerve. He also considered the choroid as a true tunic covering the retina and was of the opinion that some of its vessels pass over to the internal layer, conveying nourishment to it. Galen thus believed in the existence of a direct communication between the choroid and the central retinal artery. Though these concepts are at variance with our present knowledge, it is noteworthy that with the methods available at that time these anatomists recognized the correct topographic position of the choroid, as can be seen from the diagrammatic reconstructions of Villard.[4]

Since there were practically no new anatomical investigations during the Middle Ages, the description of the ocular structures given by the ancient Greeks was accepted by all their successors * until the Renaissance. With the Revival of Learning in Europe, observers began to identify the vessels engaged in the supply and drainage of the choroid and to study the elementary structures that take part in the integration of this coat.

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* References 5 and 6.

The first advancement beyond the previous descriptions is represented by the original work of Vesalius [7] and Casserius,[8] who in their anatomical plates reproduced small portions of the vessels extending into the choroid after piercing the sclera.

Stenon [9] was the first to recognize the venous character of the vortex veins, which in his description he called vasa vorticosa, or vortices vasculosi. Hovius † likewise considered these vessels to be veins, as can be seen by the name ductus oculorum abducentes that he gave them. This Dutch physician also noted the presence of the choriocapillaries and in them the capillary stars, which arise from the sudden division of the terminal choroidal arterioles.

The investigations of Ruysch ‡ were made on injected specimens of calf eyes. By slight manipulation he was able to detach the choriocapillaries from the larger, and external, blood vessels. On the basis of his observations, Ruysch believed that the choroid was composed of two layers, the external venous and the internal arterial, to which his son gave the name of membrana Ruyschana "in patris honorem." He also considered the vortex veins to be of arterial nature, and his descriptions were repeated by other anatomists.

It was not until the work of von Haller [15] that the existing chaos was clarified and the terms arteria ciliaris and vena vorticosa were used with their present connotation. This observer also did a chronologic review of the work of his predecessors, and it is after his name that the layer of larger choroidal vessels is called.

In injected animal specimens Winslow [16] noted a great number of vascular stars on the inner surface of the choroid. These stellate capillary structures are at present designated as "stars of Winslow." They are considered to be particularly evident in ruminants, have also been observed in rabbits, but are absent in man.

With a fine monograph, Zinn [17] further helped to clarify the nature of the choroidal vessels. His name is associated with the arterial circle of the optic nerve (circulus arteriosus nervi optici), formed in the sclera by circular anastomoses of the short posterior ciliary arteries. He described the recurrent choroidal arteries, which had previously been mentioned by von Haller and afterward forgotten.

Sœmmerring § stated that the only manner of transition from arteries to veins is through the capillaries. In his pictorial representations, this consummate anatomist exhibited the arrangement of the ultimate vascular ramifications. The numerous and excellent plates that accompany Arnold's || work helped to clarify the structure of the choroid by demonstrating the minute anatomy of this coat in great detail. Here it is pertinent to point out that the term choriocapillaries was first introduced into medical literature by Eschricht.[22]

After filling the vascular constituents of the eye with an opaque medium, Brücke [23] described blood vessels which do not terminate in capillaries, but which, after having reached a certain degree of fineness through division, curve around to empty directly into the branches of the vortex veins.

Leber ¶ denied the existence of this arrangement, and, after injection of transparent substances into the arteries, he could reach the veins only through capillaries. We are indebted to this author for a most lucid and critical description of the blood vessels and the circulation of the choroid. His monograph has been followed in the main by many other investigators. As a result of his original studies, Leber estab-

† References 10 and 11.
‡ References 12-14.
§ References 18 and 19.
|| References 20 and 21.
¶ References 24-26.

lished the constant presence of backward-coursing branches (arteriae recurrentes) that supply the anterior portions of the human choroid. These vessels had been described by Sappey [27] and Müller # but were considered only as interesting anomalies.

Our knowledge of the minute structure of the choroid was further extended by the studies of Fuchs,[30] Nuel,[31] and Passera,* each of whom applied his efforts to particular structures. Fuchs described in great detail the peculiarities of the vortex veins; Nuel undertook the microscopic investigation of the choroidal vascular arrangement in the posterior segment of the eye, and in the description of Passera primary importance is given to the study of the choriocapillaries.

An important step toward the understanding of the histology of the choroid was made in the classical work of Sattler,[34] after whom the layer of small vessels was named. The study of the cellular architecture of the choroidal vessels has been advanced by gradual accumulation of numerous detailed observations, such as, for example, those by Henle,[35] Wolfrum,[36] Salzmann,[37] Schaly,[38] and Kolmer and Lauber.[39]

In recent years investigations have been carried out to elucidate whether or not arteriovenous anastomoses are present in the choroid. That such is the case is the conviction of Loewenstein † and Orbán and Kiss,‡ who arrived at their conclusions by analogy of their findings with those in other parts of the body. However, Ashton § pointed out that this concept is erroneous, and by a series of experiments he ruled out the presence of such anastomoses, demonstrating that the areas where they have been described give only an illusory impression of direct transition.

Magitot ‖ estimates that more than half of the ocular pathology is a consequence of disturbances that develop in the layers of the choroid. If it is permissible to agree with this statement, more than ample justification can be found for our work, in which we attempted to increase the present knowledge of the basic properties of the choroid.

II. METHODS AND MATERIAL OF INVESTIGATION

The present knowledge of the structural and functional integration of the choroid has been built up progressively by studies in vitro and in vivo of human and animal specimens. The experimental procedures employed are in practice usually combined, and it is only for descriptive clarity that they are referred to separately in the following classification.

I. Studies in enucleated eyes
   1. Dissecting methods
      (*a*) Gross macroscopic examination
      (*b*) Microscopic dissection: teasing technique
   2. Histological methods
   3. Injection methods

References 28 and 29.
* References 32 and 33.
† References 40 and 41.
‡ References 42 and 43.
§ References 44 and 45.
‖ References 46 and 47.

II. Studies in vivo
  1. Indirect methods: manometric and tonometric studies of the intraocular pressure
  2. Direct methods
    A. Observations through the inner choroidal surface
      (*a*) Ophthalmoscopy
      (*b*) Biomicroscopy
    B. Observations through the outer choroidal surface
      (*a*) Dehydrated sclera
      (*b*) Scleral windows

Dissecting Methods

Gross Macroscopic Examination.—The method consists in the study of untreated and unstained specimens; it probably represents the oldest procedure, and the one by which earlier anatomists obtained all their data. By this principle, the general features of the choroid are examined through simple inspection (topographic position, boundaries and limits, attachments, and so on), while the other coats of the eye are dissected away. For this purpose, several techniques have been described by Shaw,[45] Campbell,[49] Walmsley,[50] Grant,[51] and many others.

Microscopic Dissection: Teasing Method.—This procedure yields more complete information concerning the course of the choroidal vessels than does the preceding one. It was devised by Vieussens [52] for the investigation of the central nervous system, and in the hands of Sattler [34] it furnished most significant results in the study of the middle ocular coat. He removed fresh specimens and, under a magnifying system, by careful teasing and tearing, followed the individual choroidal layers and vessels. In this way, the respective origins, courses, and terminations of the vessels were studied. The method was also used by Salzmann [37] and Vilstrup,¶ and in their work an account of the technique can be found.

Histological Methods

The study of the choroid by these methods follows closely the general principles applied for the investigation of tissues in other parts of the body. The eye can be prepared for microscopic examination by the paraffin, celloidin, or freezing technique, and the sections obtained are stained with different combinations of dyes. A great body of knowledge has been accumulated with regard to this subject and can be found in the works of Berger,[56] Seligmann,[57] Carleton,[58] Knuesel and Vonwiller,[59] Mallory,[60] and others.

The thin slices of tissue obtained permit the study of the cytological architecture of the choroid and also allow the investigation of the vascular arrangement, classically described in three superimposed strata. The inconvenience of sections lies in that the general appearance of the choroid is like a mass of blood vessels cut longitudinally, obliquely, and transversely, and from this appearance it is impossible to reconstruct the course and relations of individual units.

Injection Methods

It was pointed out by Ranvier [61] that under the heading of injections are included procedures by which substances are introduced into the body for a variety of purposes. Such injections were used to demonstrate the circulation, to test the response after the introduction of substances into the vessels of living animals, to fill large cavities of the body, and for other designs described in the historical review of Cole.[62] In the present study, the definition of Robin # will be followed, and

¶ References 53-55.
# References 63 and 64.

reference will be made only to those techniques that make known to us the absolute vascularity of the choroid.

Ruysch * is considered the exponent of the injection method, and apparently he was the first who succeeded in obtaining extensive injections of the capillaries. One of the first to inject successfully the microscopic vessels and to make corroded preparations was Lieberkühn.[65]

(*a*) *Injection Masses.* — The first media employed were liquids, used by Berengarius,[66] and air, used by Massa,[67] during the 16th century. Swammerdam [68] is rightly credited with being the inventor of the solidifying injection masses, although Boyle [69] and Pecquet [70] came out with prior publications. Since these early works, a great variety of compounds have been used for the injection of blood vessels, and an extensive reference to them can be found in "Lee's Vade Mecum." [71]

Injection masses are frequently composed of a vehicle and a coloring substance with which it is combined. Since the time of Boerhaave,[72] it was commonly noted that the vehicle will enter the small vessels, while the colored agent remains behind.

In recent years, and for the study of the choroid, Vilstrup † used a polyallyl ester resin for injection into experimental animals. Ashton ‡ prepared human choroidal specimens with liquid latex. The use of latex for injection of vertebrate vessels was first described by Hill.[73] This method was employed by us for injection of the rabbit's choroid. Our results have not been completely satisfactory because of the incomplete filling of the vascular bed, permitting only observations of the larger vessels. Other compounds will be tried in the future.

When possible, it is advisable to flush the vessels with water before throwing in the injection mass. Bartholin § was the first to advocate this step.

(*b*) *Route of Administration.*—In human eyes the masses can be injected through the ophthalmic artery after removal in toto of the orbital content and the cavernous portion of the internal carotid.

In smaller mammals, such as those used for experimental purposes, larger vessels leading into the choroid are employed for the injection. One or both carotid arteries can be injected with or without preceding ligature of the jugular veins. In general, retrograde venous injections have given less satisfactory preparations.

(*c*) *Injection Technique.*—The substances used are introduced into the vascular system under pressure. Lusitanus [76] filled vessels by means of air pressure supplied from the mouth. An injecting syringe with cannula of the modern pattern was first employed by de Graaf.[77] Hales [78] used an apparatus by which the force of injection was known and kept constant. This technical refinement is still valid and can be accomplished by electric pumps (Ashton ‖), regulated pressure from gas cylinders (present investigation), and many similar devices (Ranvier,[61] Robin,¶ Beale,[79] Fol,[80] and others).

It is necessary to have a container to be filled with the injection mass interposed between the pressure apparatus and the specimen. This arrangement permits the discharge of the substance, as well as the control of its flow. Through the inlet of

* References 12-14.
† References 53-55.
‡ References 44 and 45.
§ References 74 and 75.
‖ References 44 and 45.
¶ References 63 and 64.

the container pressure is transmitted to the mass, and by the outlet it is allowed to escape into the preparation through metal needles or glass cannulas.

(*d*) *Dissection Technique.*—After injection, the specimens are fixed with adequate solutions that harden the injected compounds. Acetic acid 4% and/or formaldehyde solution U. S. P. 4% have been recommended for latex; formalin and mercury bichloride solution for resins; water for celloidin, and so on.

The next step is to open the eyeball. For this purpose an incision through all coats is made parallel to the corneal limbus, at a distance of from 2 to 3 mm. Through the incision a blade of a pair of scissors is introduced into the eyeball; by a circular cut the eye is divided into an anterior portion, containing the cornea, lens, and ciliary body, and the posterior portion, containing the choroid and other structures.

The gelatinous vitreous body and the retina are brushed away carefully, without damaging the underlying structures. The removal of vitreous can be facilitated by leaving the specimen in saline solution for one to two hours.

The choroid is detached from the sclera with a spatula inserted in the suprachoroidal space by running it in all directions. The vascular and nervous connections, with the outer coat, are severed, and the isolated choroid is floated out.

(*e*) *Corrosion and Digestion Procedures.* — Some of the earliest corrosion preparations were made by Bidloo [81] and Cowper [82]; the idea was inspired by the excarnations of Glisson.[83]

Corrosion with strong solutions (hydrochloric acid, nitric acid, and others) is in general not recommended for choroidal specimens, because they produce curling and distortion of the specimens. Instead, maceration in organic juices (digestion) has been more valuable. The most frequently employed enzymes are pepsin (in 0.1 N hydrochloric acid) and trypsin (in 10% sodium bicarbonate). The injected specimens are incubated in the former solution for 48 hours at 37 C and then for a similar period in the latter solution.

When indicated, the digested choroid can be cleared with potassium oxalate 2% (for 15 to 30 minutes), followed by washing in oxalic acid 1%. When albino rabbits are used, the specimens do not have to be carried through a process of depigmentation.

(*f*) *Staining Procedures.*—Bleached choroid can be stained with hematoxylin and eosin, hemalum, and other dyes, following the usual techniques.

(*g*) *Mounting Procedures.*—Since the choroid represents a spherical curved body, it may be studied as a whole in a glass sphere of the same size as the sclera.

To get flat-bulk preparations of the choroid and to obtain its spread into an even plane with minimal distortion, the detached specimen may be divided into several segments.

The preparations can be examined either in dry state or after having been cleared and mounted in polystyrene or glycerin. Injected specimens can also be studied by dissection and used for histological sections.

Indirect Methods of Observation

The principle of these methods consists in measuring the intraocular pressure by manometry or tonometry and correlating the variations of the intraocular pressure with vascular events after elimination of other factors. The best integral knowledge of the uveal circulation and the most extensive literature on alterations in the size of the vessels have been accumulated by the use of these procedures.

Details of the technique have been discussed in the contributions of Adamuek,[84] Leber,# Hoeltzke,[85] von Schulten,[86] Bellarminoff,[87] Parsons,[88] Henderson and Starling,[89] Wessely,* Rochat,[94] Seidel,[95] Bliedung,[96] Colle, Duke-Elder, and Duke-Elder,[97] Davson and Purvis,† Guerry,[100] and many others.

The study of the circulation in the middle ocular coat by these methods has limitations. In order to estimate alterations in the state of the vessels, it is necessary to eliminate changes in other structures, and this is not always easy to achieve or interpret.

Direct Methods of Observation

Alterations in the size of the choroidal vessels can be determined in albino animals by observation of the vascular coat from its inner (retinal) or its outer (scleral) surface.

1. *Study of Choroidal Vessels from Their Retinal Aspect.*—This consists in the application of the same principles that constitute the basis for the examination of the fundus by ophthalmoscopy and biomicroscopy.

Ophthalmoscopic Methods: The technique of indirect ophthalmoscopy employed by von Schulten [86] and the use of a Gullstrand ophthalmoscope by Cohen and Bothman [101] are sufficient to illustrate this group.

Biomicroscopic Methods: Koeppe [102] was the first to publish a method for examination of the fundus of the eye under high magnification by means of a slit lamp. The investigation of the choroidal vessels in animals was accomplished by Zwiauer and Bornschein,[103] who applied the principles established by Lambert [104] and Porsaa.[105] The retinal and choroidal circulations were observed through a horizontally placed microscope furnished with a lens holder for a contact glass. This is to be inserted in front of the animal's eye and neutralizes the curvature of the cornea.

These methods suffer from some handicaps. The study must be made through the pupil, which will vary in size when drugs are tested, thus restricting the field of observation. Motion of the animal also interferes with observation. Furthermore, the study of the vessels is made under comparatively low magnification (the maximal reported is about $\times 60$), so that their measurement cannot be absolutely relied upon. The procedures under consideration have the advantage of maintaining the eye under conditions that more closely approximate a physiological norm.

2. *Investigation of Choroid from Its Outer Surface.*—This is possible only after the scleral tissue is made transparent or a window is inserted. The following were the principal methods employed in the present investigation, and for this reason they will be described in detail.

Dehydrated Sclera: The first observations of the choroidal circulation through the dehydrated sclera of the proptosed eyes of albino animals were made by Waller.‡ The transparency of the dehydrated sclera was also described by Leber, previously cited, who noted a similar change of the sclera in cholera patients, an observation that was corroborated by Birnbacher and Czermak.[109] Fischer [110] did extensive studies on the origin of the transparency of the sclera in the proptosed eye of the rabbit and concluded that it was due to loss of water content. This technique was used by Kahn [111] for spectroscopic studies of hemoglobin, and in

References 24-26.
* References 90-93.
† References 98 and 99.
‡ References 106-108.

recent years the method was tried again with its original purpose by Leopold [112] and Greaves and Perkins.§

Technique. (1) First stage. Preliminary maneuvers; preparation of animal.

(*a*) The animal is anesthetized, and the whiskers are trimmed.

(*b*) The animal is placed on its side; the eye to be operated on is turned up and at a level with the operator's gaze.

(*c*) A suture (0000) is then placed through the upper lid, and a hemostat attached to it is allowed to hang in the air. This provides good exposure of the sclera above the limbus.

(*d*) When necessary, medial and lateral canthotomies can be performed.

(2) Second stage. Incision of the conjunctiva.

(*a*) The nictitating membrane is dissected.

(*b*) An incision is made in the conjunctiva and Tenon's capsule 8 to 10 mm. from the limbus, in the cul-de-sac, between the medial and the superior rectus.

(*c*) The conjunctiva is dissected from the sclera back to the limbus over the area selected for observation.

(*d*) A suture (0000) placed through this conjunctival flap and a hemostat attached are used to hold the eye in the desired position.

(*e*) The medial and superior recti may be cut close to their insertion when they interfere with observation.

(3) Third stage. Dehydration and clearing of the sclera.

(*a*) By leaving the bare sclera exposed to air for some time, or by directing to it a stream of warm air for a short interval, a red patch appears, which indicates that the sclera has been rendered transparent by dehydration.

(*b*) The optical conditions can be improved by applying to the sclera a few drops of immersion oil or glycerin. Both substances were tried by us, without alteration in the comparative behavior of the vessels.

Comment. The method described is simple and permits the visualization of large areas of the choroid, but has the disadvantage of producing ocular dehydration and consequent hypotony, introducing thus alterations in the physiology of the eye.

Scleral Window: The examination of vessels in living animals through transparent windows was first accomplished by Sandison.‖ The method was suggested by the glass-chamber studies of Ziegler,[117] and the original work was begun and carried out under the direction of E. R. Clark.¶ This investigator, with E. L. Clark, has since devised further improvements and refinements of the procedure by which he has been able to accumulate considerable information on the small blood vessels of the body.

Windows have also been devised for the observation of the circulation in more protected organs. This type of work can be exemplified by the investigations of Forbes and co-workers # and Wentsler,[122] on the brain, and of Zintel,[123] on the intestine.

In the field of ophthalmology, Elschnig [124] described a scleral flap that he called a scleral window for access to foreign bodies in the ciliary body and vitreous.

§ References 113 and 114.
‖ References 115 and 116.
¶ References 118 and 119.
# References 120 and 121.

Bailliart [125] trephined the sclera and then applied drugs for the study of the retinal vessels, but he almost always injured the choroid and allowed bulging of this coat.

Leopold [112] was the first to devise a scleral-window technique for observation of the choroidal circulation in the rabbit's eye, and a similar procedure was later used by Cook and Ashton.*

Technique. (1) A procedure similar to the one previously described for dehydration of the sclera is followed up to the second stage.

(2) Third stage. Scleral incision.

(*a*) The best position of the window for illumination is from 4-6 mm. behind the limbus. It is also convenient that the window be so placed that it will be situated over one of the arterial branches that can be observed by transillumination with a strong light. Usually the selected place will be approximately halfway between the nasal long posterior ciliary artery and the point at which the superior medial vortex vein leaves the sclera.

(*b*) A scratch-down incision, approximately 3 mm. in length and perpendicular to the limbus, is started in the sclera. The cut is made diagonally, and its completion should not be attempted at this point. The incision can be made with a scalpel, keratome, or sclerotome tip.

(*c*) Two or three preplaced sutures (000000) are put in the edges of the scratch; a single horizontal mattress suture is usually easier to apply. At this time the suture to be used through the trephine is also placed in the point where the orifice of the window is to be located. Insertion of the trephine suture before completion of the incision makes undue manipulation unnecessary after the plastic is inserted; such manipulation was found to cause bleeding beneath the plastic in some occasions.

(*d*) The scleral incision is then carried carefully down to the choroid. The choroid appears as a glistening membrane in the scleral fiber meshwork at the line of the incision. Minor bleeding is easily stopped by pressure. It does not seem to preclude a good window, but such a window is usually not as clear (Fig. 1*a*).

(*e*) When the uveal tissue is reached, the wound is enlarged with scissors. One blade of a small blunt straight scissors is carefully inserted under the sclera at the edge of the incision and the wound enlarged by cutting to each side.

(3) Fourth stage. Insertion of plastic.

(*a*) A plate of transparent plastic,† 3.5 by 4.5 mm. in size, is then prepared. The edges of the plastic are smoothed and rounded with emery paper.

(*b*) A narrow spatula is then carefully introduced through the scleral wound and pushed forward, hugging the scleral inner surface. The spatula is run up and down to remove any fibers (Fig. 1*b*). Bridging fibers are not usually found in the albino rabbits, and the instrument passes very easily between the choroid and the sclera.

(*c*) Traction is applied to the preplaced scleral suture; the lip of the incision under which the plastic is to be slipped is held up with one hand. The plate, held with a forceps in the other hand, is gently inserted under the sclera (Fig. 1*c*). During this insertion the plastic is allowed to hug the scleral side and is passed between the sclera and the choroid until the entire length of the plate is in the

* References 44 and 45.

† Transparent plastic prepared by Eastman Kodak Company, 0.0075 in. thick.

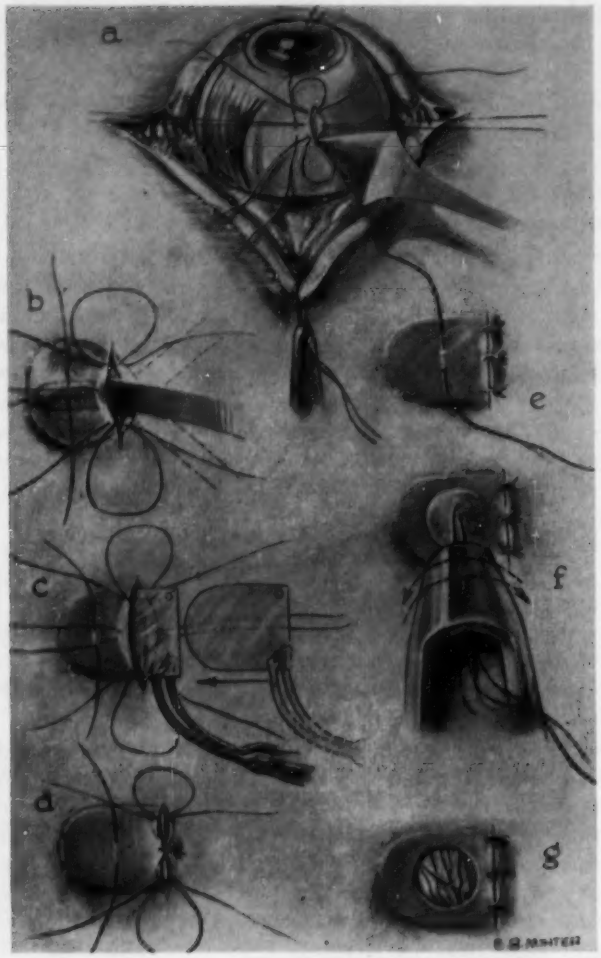


Fig. 1.—Scleral window technique. Description in text. Reproduced from article by I. H. Leopold (Tr. Am. Ophth. Soc. **49**:625, 1952), by permission of the Columbia University Press, New York.

suprachoroidal space. The plastic should not reach within 2-3 mm. of the main arterial trunks, because these vessels and their branches cross the sclerochoroidal space and can be severed if the plastic extends very far.

(*d*) The scleral incision is closed by tying the preplaced sutures (Fig. 1*d*).

(4) Fifth stage. Trephination of the window.

(*a*) The scleral suture to be used with the trephine is centrally located above the plastic plate (Fig. 1*e*). Both ends of this suture are passed through the opening of a 2.5 mm. trephine. The sclera is then trephined down to the transparent plate (Fig. 1*f*), thus forming a round window through which the choroidal vessels can be seen (Fig. 1*g*).

(*b*) If the scleral fibers are not cut entirely by the trephine, the window can be completed by careful use of iris scissors.

Comment. This type of window permits studies under somewhat more physiological conditions. The intraocular pressure is only slightly altered,[112] and hydration of the sclera with isotonic saline can be maintained without interference with the view of the vessels. The procedure has the disadvantage of requiring a delicate operation and of narrowing and limiting the fields of observations.

Material of Investigation

(a) *Animals*

The absence of pigment in albinotic eyes was first proved by Duddell [126] and specifically mentioned in the rabbit by Monro.[127] In order to demonstrate the images formed in the eye, Magendie [128] made use of the lack of pigment in albino animals; this same property permitted our investigations in vivo and facilitated the studies after enucleation.

Fig. 2.—Special table provided with holders to immobilize rabbits.

Observations were made almost entirely in mongrel albino rabbits, which had a weight varying between 2 and 4 kg. They were anesthetized with intravenous pentobarbital sodium (0.45 ml/kg.), chloroform, or ether. No noticeable difference in the behavior of the vessels was observed after the use of these various anesthetic drugs. On the basis of this observation and for its obvious advantages, the intravenous method was most frequently employed. Here it is pertinent to note that the anesthetics mentioned have been described as having variable vasomotor effects in different vascular areas. In particular, pentobarbital sodium was reported by Richter and Oughterson [129] to induce peripheral vasodilatation in dogs, but in our present study it was impossible to eliminate this factor because of the technical difficulties associated with observations in unanesthetized animals.

Some studies were made in albino guinea pigs and rats anesthetized by intraperitoneal injection of pentobarbital sodium.

Having been anesthetized, and after the surgical intervention was completed, the animals were placed at the edge of a table provided with a holder to immobilize the head and maintain the field of observation in position (Fig. 2).

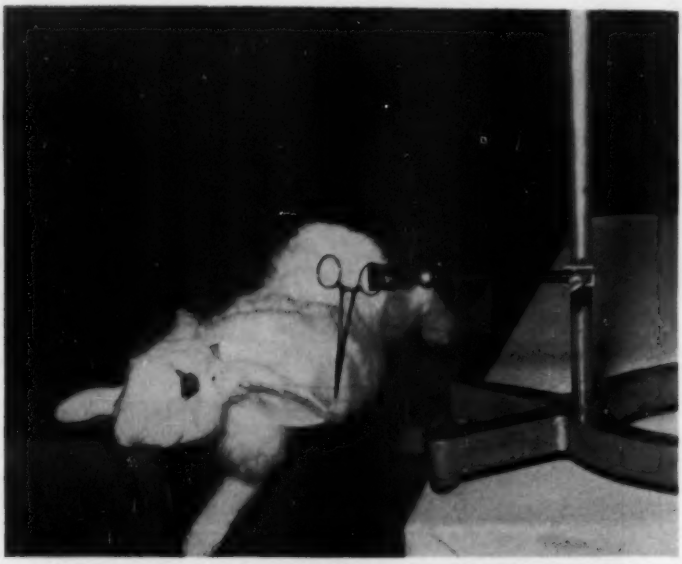


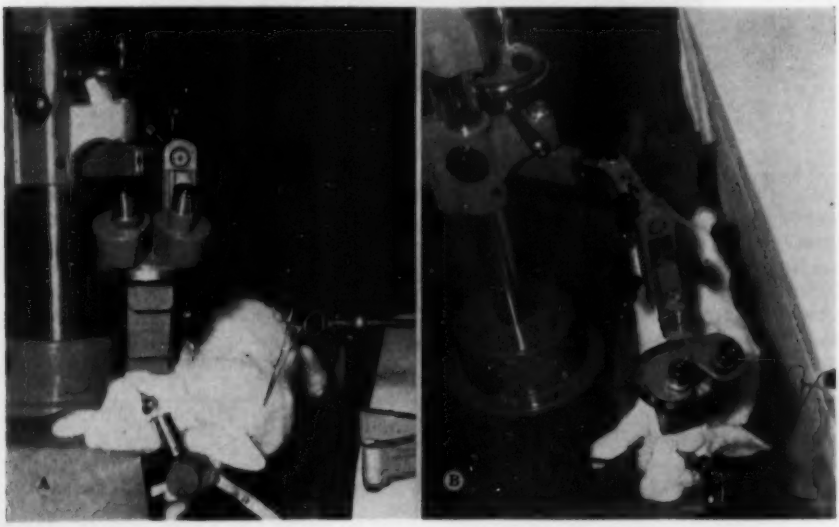
Fig. 3.—Rabbit in position. The sutures in the upper lid and conjunctiva are pulled in opposite directions. The eye is maintained with convenient proptosis by varying the traction on the sutures.

The sutures in the upper lid and conjunctiva [see First stage (*c*); Second stage (*d*)] are pulled in opposite directions. By varying the traction exerted, the eye is maintained fixed with convenient proptosis, which permits observation from above and illumination from below and through the pupil (Fig. 3).

(*b*) *Microscope*

The choroidal vessels were examined in detail through a binocular stereoscopic microscope that provides magnifications ranging between 10 and 150 diameters (Fig. 4). Slight motion of

Fig. 4.—General view of equipment ready for use. Observations are made from above through the stereoscopic microscope, and illumination is provided from below.



the animal, such as respiratory movements, made the use of higher magnification extremely difficult. Vessel caliber was judged by the use of a micrometer scale inserted in one of the oculars of the microscope. The micrometer was calibrated against a stage micrometer, so that the size of the vessels could be determined, in microns, at any time. The smallest vessels identified clearly were of about 15μ caliber and changes in caliber were noticed fairly accurately when the vascular diameter was above 25μ.

(c) *Illumination*

Bright focal illumination to observe the desired choroidal area was accomplished with a Barkan light or a Nicholas illuminator. To reduce the heat, a disc of heat-resistant glass can be adapted to the system. A device similar to the quartz-rod technique of transillumination suggested by Knisley and others‡ would probably be very useful.

(d) *Photography*

Photographs were obtained through an Exakta VX camera mounted in a microscopic adapter. This arrangement permits the taking of a series of exposures without disturbing the apparatus. Eastman Kodak Plus-X film was used with exposures of 2-4 seconds. It was found that for accurate comparisons it is necessary to keep the exposures and the illuminations constant throughout the experiment, as slight differences in the photographic technique sometimes produce misleading appearances of the vessels. Besides the usual black and white photographs, it was possible to obtain color plates using an Eastman Kodachrome film exposed for approximately 8 to 10 seconds. Cinematographic records were accomplished with a Pathe Super 16 camera using Kodachrome Type A film.

III. ANATOMICAL OBSERVATIONS

The comparative anatomy of the choroid in mammals is fairly uniform (Sattler,[84] von Schulten,[86] and others), and thus its study in lower animals helps in the understanding of the structure and behavior of this coat in humans.

Anatomical descriptions of the choroid and related vascular elements in the rabbit were given by Krause,[132] Virchow,[133] Henderson,[134] Davis,[135] Akagi,[136] Vilstrup,§ and others. The last-mentioned investigator has recently covered the subject in an extensive manner.

In the present study, our primary objective is to outline the appearance of the middle ocular coat as it is visualized in the living animal. Short reference will be made to the vessels not seen in vivo, so as to give a more integrated picture of the ocular blood supply. Such a description is especially valuable because it will enable one to understand the correlation between the dynamic aspect of the circulation and the type of structural element in which changes occur. For this purpose the vascular elements of the choroid will be described from their arterial departure to their venous end.

Arteries.—The ocular blood supply in rabbits is derived from the common carotid artery. This vessel, at the level of the hypoglossal nerve in the neck, divides into the internal and external carotid arteries.

The internal carotid is much the smaller, enters the skull through the carotid foramen, and, after crossing the oculomotor nerve, gives off the internal (or superior) ophthalmic artery.

The external carotid, below the neck of the jaw, branches into the superficial temporal and the internal maxillary. The latter runs deep to the internal pterygoid behind the jaw; it then passes the pterygoid canal and gives off the external (or inferior) ophthalmic artery.

‡ References 130 and 131.

§ References 53-55.

Ophthalmic Arteries: The internal (or superior) ophthalmic artery is but little developed. It enters the orbit through the optic foramen and goes through this on the inferior and lateral side of the optic nerve; then it winds under the nerve to its anterior aspect and anastomoses with the external ophthalmic artery.

The strongly developed external (or inferior) ophthalmic artery runs along the anterior surface of the upper part of the great wing of the sphenoid, bends forward over the optic nerve, and reaches its anterior side. It there anastomoses with the internal ophthalmic artery.

The posterior ciliary arteries originate from the ophthalmic main stems or from their anastomoses. They carry the entire blood supply to the uvea, because in the rabbit no anterior ciliary arteries are present.

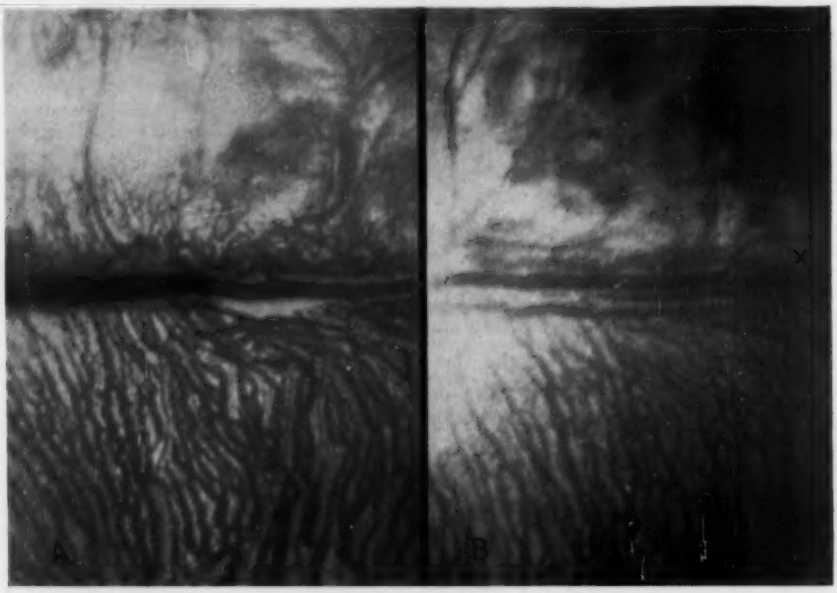


Fig. 5.—Appearance of the choroid in living rabbits. *A*, the long posterior ciliary artery appears as a straight, dark trunk that runs in the horizontal meridian of the eye. Above this artery there is a clear zone with very few large vessels. *B*, photomicrograph from a different animal, showing an area anterior to the previous. At *X* the long ciliary artery divides into two terminal branches, which will go to form the major circle of the iris. Reduced to 65% of mag. × 10.

Long Posterior Ciliary Arteries (Fig. 5): These vessels appear as single stems that, after departure from the main arteries of the eye near the optic nerve, run in the horizontal meridian on either side of the eye (nasal and temporal arteries).

The initial portion of the vessels is located outside the eyeball and has an irregular contour and a diameter that varies between 400μ and 250μ. The arteries enter the suprachoroid by piercing the sclera slightly behind the equator through a canal that appears to run obliquely. In the choroid the arterial trunks travel straight forward; their contour becomes regular; a central light reflex is usually clearly visible, and their diameter measures 250μ to 150μ.

At a variable distance from the iris, the long posterior ciliary arteries divide into two terminal branches (200μ-100μ), which diverge in opposite directions to

form the major arterial circle of the iris (circulus arteriosus iridis major). This arterial ring can be seen at the periphery of the iris. From it, recurrent branches depart and run back through the ciliary body, and, without anastomosing with the ciliary arteries, they terminate in capillaries.

Around and dorsal to the long ciliary stems in their intraocular course there are areas of variable size that appear poorly vascularized. Only few vessels cross the central portions of these fields of observation, which, under high magnification and between the circulating blood, have a honeycomb appearance, stippled with numerous minute white spherical bodies, whose nature and exact position could not be determined. Many terminal arterioles and collecting venules are present at the peripheral boundary of these zones.

Short Posterior Ciliary Arteries: These arteries depart from the main ophthalmic stems and the long posterior ciliary arteries, from which usually three to eight branches originate.

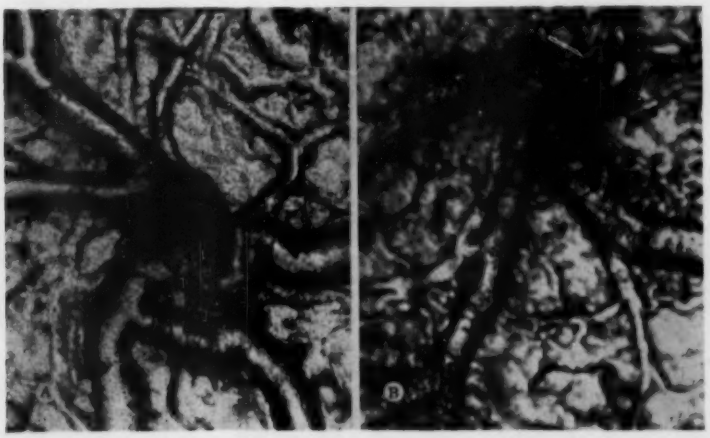


Fig. 6.—Choroid of rabbit injected with neoprene. Survey of the area corresponding to the entry of short ciliary arteries around the posterior segment of the eye. These arteries divide into divergent branches, giving a stellate appearance to the whole. Reduced to 56% of mag. × 100.

Most of the short ciliary arteries soon divide during their forward course toward the eye, and their number increases up to 15 or 18 vessels. Posteriorly their perforation of the sclera is less oblique than anteriorly. This is because the wall of the sclera is more perpendicular to the trajectory of the vessels the more posteriorly they meet. The scleral perforations made by the short ciliary arteries are distributed in a flat arc, which extends from the entrance of one long ciliary artery to the entrance of the other. Near the posterior pole this symmetry is disturbed by the presence of perforations in and around the foramen of the optic nerve. Here, usually two to three arteries are seen to enter. They give off a great number of fine branches that take a circular course around the optic nerve, taking part in the formation of the vascular ring round the foramen of the nerve.

The short ciliary arteries, when entering the choroid, can be described in the following groups:

(*a*) Arteries that enter proximal to the posterior pole can best be studied in injected specimens. These vessels commence branching within the sclera itself and

the suprachoroidal space; the resulting branches diverge radially, giving a stellate appearance to the whole (Fig. 6). These vessels eventually run forward through the upper and lower halves of the choroid and during their course divide dichotomically and monopodially, developing finally into arterioles.

(*b*) In living animals, distal to the pole some of the short ciliary vessels are seen to originate monopodially from the long ciliary arteries, usually before these enter the suprachoroidal space. Sometimes the long arteries give off branches during their intrascleral course or immediately after they enter the choroid, but after this no collaterals originate before the vessels get near the ciliary body. Here, as a rule, one or more fine arterioles are given off and take a circular course along the anterior margin of the ora serrata. These small vessels can be seen to anastomose with each other, but not with the recurrent branches from the major circle of the iris.

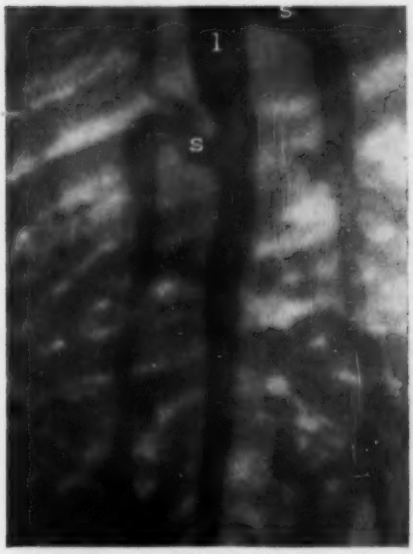


Figure 7

Figure 8

Fig. 7.—Appearance of the posterior ciliary arteries in the choroid of living rabbits. The short ciliary arteries (*s*) are seen to originate monopodially from the long ciliary (*l*). Shortly after their origin they suffer an angulation of a variable degree and become parallel to the main stem for some distance. Reduced to 60% of mag. × 40.

Fig. 8.—Photomicrograph from a different animal, showing an area anterior to the one in the previous picture. The short ciliary arteries give off side-collaterals (*c*) almost at right angles, while the long ciliary artery remains without branching. Reduced to 60% of mag. × 40.

Among the short ciliary arteries that enter anteriorly (Group b) strong vessels (200μ-100μ) are often seen to be arched because shortly after their origin they suffer an angulation of a variable degree. The change in direction may be up to 90 degrees, and when this occurs the vessels described become parallel to the long ciliary arteries for some distance; during this course they give off side-collaterals almost at right angles that run upward and downward parallel to the equatorial plane of the eye (Figs. 7 and 8).

Other branches derived from the long ciliary arteries run transversely or posteriorly and again give off collaterals similar to the ones just mentioned.

Eventually all the arterial branches, regardless of their point of origin, seek the intervenous spaces and are oriented in a direction that points toward the vortex veins.

Arterioles.—According to Ham,[137] arteries with a caliber of 100μ or less are generally called arterioles. Although the over-all diameter may not be the most important characteristic in determining whether a given vessel is an arteriole or not,‖ it was the only criterion available in our study, and for this reason it was followed.

The choroidal arterioles originate from and are in direct continuity with the main ciliary vessels. The arterioles reach for the intervenous spaces and are situated deep between the veins. Hence we find the arterioles and venous channels in close neighborhood with each other and covering the major part of the choriocapillaries (Fig. 9).

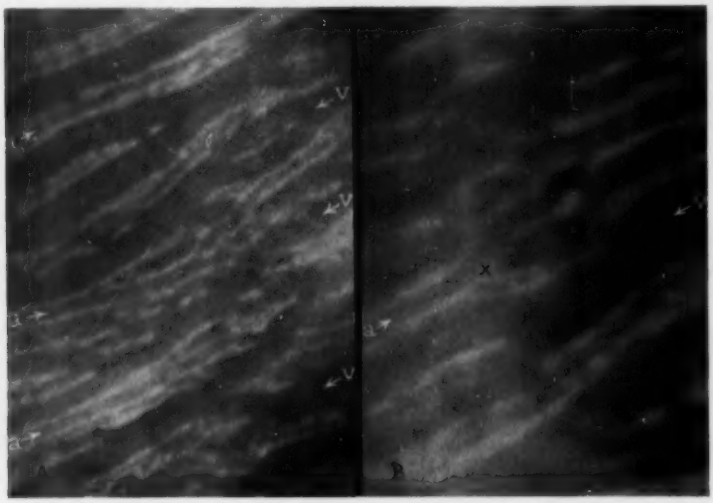


Fig. 9.—Appearance of the choroid near the equatorial zone (living rabbit). The slender arterioles (*a*) are seen between the veins (*v*). Note that the arterioles cross from one intervenous space to the neighboring interspace and produce indentations in the venous wall (*x*). Reduced to 55% of (*A*) mag. × 40; (*B*) mag. × 75.

The arterioles can be identified in living animals because they are slenderer and have a lighter color than the neighboring veins; they appear as straight cylindrical rods that not infrequently give off side-branches monopodially almost at right angles or divide dichotomically at acute angles (Fig. 10). By the latter manner of division the areas supplied by the arterioles become wider the farther distally the vessels run. Either one or both of the arterioles resulting from the vascular branching leave the original intervenous space and cross the veins in order to reach the neighboring space. During this crossing the arterioles lie directly against the venules and will often produce a slight indentation on the latter.

When the arterioles situated in the intervenous spaces approach a vorticous center, they may behave in two ways: (*a*) Either they may disappear under the conglomerate of veins, or (*b*) they may cross superficially to one or more venules,

‖ References 138 and 139.

describing a semicircle, and then run within the intervenous space in an opposite direction from the one they originally had.

The walls of the arteries and arterioles described can be seen as thin, transparent lines, in which no structural elements are identified. They can be made more apparent when polarized light is used.

Terminal Arterioles: Under this name Chambers and Zweifach [140] considered those arterioles that in the mesentery of animals have a diameter of less than 20μ to 30μ during their partially constricted state. In her work Vilstrup ¶ describes two types of terminal branches: (*a*) The first type is characterized by short and broad stems (30μ-60μ), connecting larger vessels with the choriocapillaries; (*b*) the second type consists in long and slender vessels (6μ-8μ), which form a fine network situated on the outer surface of the capillary net.

Under the conditions of our experiments in living animals it was not possible to determine with certainty the anatomical characteristics of these vessels.

Fig. 10.—Arteriole giving off a side-branch monopodially almost at a right angle (*m*) and dividing dichotomically at an acute angle (*d*). Reduced to 70% of mag. × 40.

Choriocapillaries.—The choriocapillaries form a membrane extending through the entire choroid to the ora serrata. This network is situated in a single layer and with a depth of only one capillary. When it is observed in vivo and from its outer aspect, the greatest part of its surface is seen to be covered by the layers of large and small vessels. In the open vascular fields around the long posterior ciliary arteries, which were previously described, the flow of blood in the minute vessels was observed. In these areas the blood appears to form a thin layer of erythrocytes, which while moving reflect the light at different angles, thus creating the impression of scintillating stars on a well-illuminated background. No vascular walls were identified in these observations; hence it was not possible to establish with certainty the nature of the vessels through which the flow was occurring.

Collecting Venules.—The origin of these vessels from the membrana choriocapillaris, so well studied in the injected specimens, could not be made out in living animals. In portions of the clear zones several streams of erythrocytes were seen to have convergent directions; then they rapidly unite to form larger vessels (about 50μ), which drain into larger neighboring veins (Fig. 11).

¶ References 53-55.

Fig. 11.—Veins (*v*) around the clear areas. These vessels are seen to have a convergent direction, forming progressively larger stems. Reduced to 82% of mag. × 40.

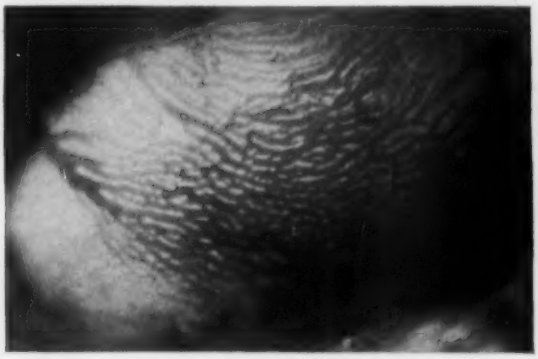
Veins.—The medium- and large-sized veins form the typical vascular component of the choroid. These vessels appear as thick ribbons with numerous anastomoses at wide angles, and they are convergent toward centers represented by the vortex sinuses. The venous stems have in the midportion of their trajectory a width of about 75μ to 150μ; they grow rapidly in caliber and by continuously merging form 3 to 12 trunks, which near the vortices measure 200μ-400μ and are wider than the intervenous spaces. During their course the veins are seen to receive branches from deeper layers, and in general their caliber is two to five times as large as the caliber of the neighboring arterioles.

Special mention should be made of the venous appearance in (1) the posterior part of the eye and (2) at the boundary between the choroid and the ciliary body.

(1) Posteriorly, the veins are distributed quite uniformly, and they form a broad circle surrounding the orifice, corresponding to the passage of the optic nerve.

(2) Anteriorly, and marking the margin of the choroid, is the venous circle of Hovius (circulus venosus Hovii), which consists of veins so closely packed that they appear to occupy almost the entire area, and as a result in many places it is difficult to make out the intervenous spaces (Fig. 12). In front of the venous circle the pars plana (orbiculus ciliaris) of the ciliary body can be visualized. It appears

Fig. 12.—Venous circle of Hovius, formed by a conglomerate of veins in the anterior portion of the choroid. Reduced to 75% of mag. × 10.



as pale, nonvascularized intervals separated by parallel veins, which run backward meridionally from the pars ciliaris to the anterior portion of the choroid (Fig. 13).

Vortices: The veins of large choroidal fields converge toward certain centers, giving the stellate appearance of each vortex. In the vortices there are present ampullar vascular dilatations (sinus or ampullae vorticis) that transport the blood to the vortex veins. The vortical centers are located anteriorly to the equator and lie nearer to the median plane of the eye than to the meridional horizontal plane.

Vortex Veins: In typical cases two pairs of veins are encountered: one superior and the other inferior. Each vein is formed by two to five branches, of which two are usually more distinguishable. The course of these branches through the sclera is oblique and convergent to form each of the main venous stems (Fig. 14).

Fig. 13.—In the anterior margin of the choroid the veins are closely packed, forming the venous circle of Hovius (*v*). In front of this, the following structures are successively visualized: pars plana (*p*), pars ciliaris (*c*), iris and pupil seen tangentially (*i*), anterior chamber (*a*), and cornea (*o*). Reduced to 80% of mag. × 10.

The distance between each pair of vortex veins is smaller than the distance between one of the upper veins and the nearest lower vein. The superior veins leave the sclera on either side of the superior rectus, and the inferior veins leave the globe on either side of the inferior rectus.

Each pair of veins is convergent, and they enter the orbital venous sinus, from which the blood leaves the orbit through several channels.

Choroidal Vascular Anastomoses.—The presence of interarterial and intervenous anastomoses in the choroid is a fact that has been recognized for a long time.#

References 24-26.

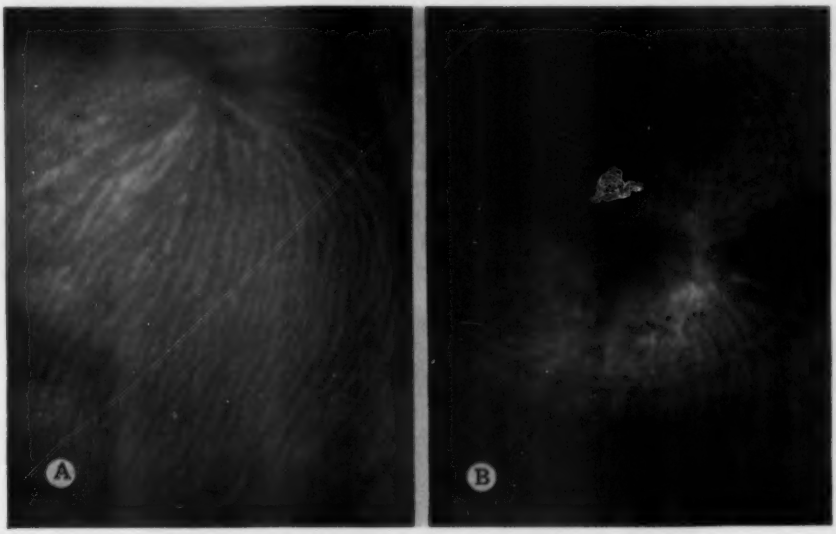


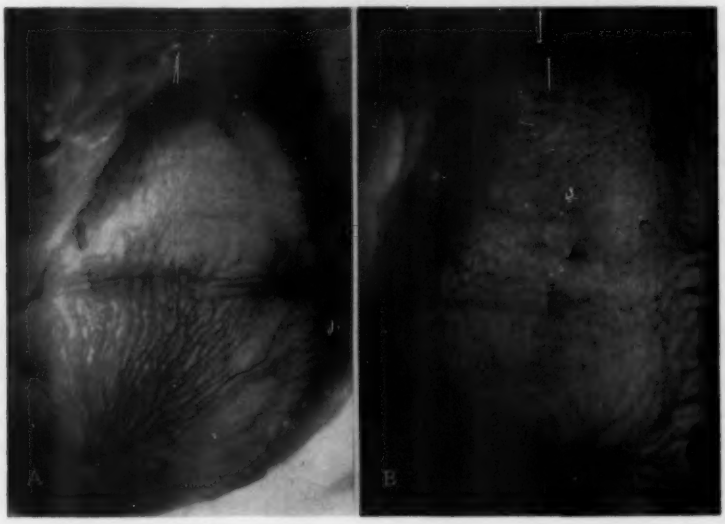
Fig. 14.—Choroidal veins in living rabbits. The vessels merge continuously to form larger trunks, which drain into the vortical areas. Reduced to 69% of mag. × 10.

It has also been the general consensus that the only way of transition between the arterial and the venous side of the circulation is through the choriocapillaries. This last statement has been challenged by Brücke,[23] Schneller,[141] Loewenstein,* and Orban and Kiss,† who assume the existence of direct arteriovenous communications.

* References 40 and 41.

† References 42 and 43.

Fig. 15.—General survey of the choroid in living guinea pigs. The ciliary arteries are located at the center of the photomicrograph and the vortex veins on each side. *A*, reduced to 53% of mag. × 10; *B*, reduced to 52% of mag. × 40. (The round transparent bubbles are artifacts.)



The first suggestions of the presence of these anastomoses was based on the study of injected specimens in which the veins were well filled while the capillary net was filled only irregularly, after the masses had been injected through the arterial system. The early observations of Leber and the more recent studies of Vilstrup ‡ have proved that this appearance is only incidental to the material and method followed for injection, and in no case were these authors able to visualize the presence of such anastomoses that would by-pass the capillary net.

The problem was revived from another angle by Loewenstein,§ who found in the choroid the presence of epithelioid muscle cells, or glomus cells. These cells have been described as the basic elements of arteriovenous anastomosis, which

Fig. 16.—Choroid of living guinea pig. The long posterior ciliary artery is in the center, appearing as a thick stem. Flanking it are the short ciliary arteries, which are thinner and have a tortuous course. Reduced to 83% of mag. × 20.

Loewenstein § therefore believes must be present in the choroid. This theory was further advanced by Orban and Kiss,|| who described circumscribed venous dilatations termed bulbiculi, localized at the arteriovenous crossings. By analogy with the work of Clara,[142] and supported by the findings of Loewenstein, these authors concluded that the bulbiculi are the site of arteriovenous anastomoses and that the choroidal circulation is controlled through them.

‡ References 53-55.

§ References 40 and 41.

|| References 42 and 43.

Ashton ¶ studied the human choroidal vessels in injected specimens and histological sections, and in no instance was he able to find vessels that would lead the blood from the arteries to the veins without passing through the capillary net. The presence of arteriovenous anastomoses was also denied by Greaves and Perkins,# who observed the circulation in living animals. In the present study we arrived at the same conclusions because in no instance were we able to observe a direct flow of blood from arteries to veins. Such an impression is sometimes created when the circulation in the smaller vessels is observed, but more careful study always permitted the separation of the flowing currents.

Comment.—After the preceding anatomical description, it is understandable why we encountered limitations in the study of small caliber vessels and why in the present work observations were made primarily on the behavior of the main arteries, their branches, and the larger veins.

Anatomic Remarks on the Choroid of Guinea Pigs.—In these animals the arrangement of the choroidal vessels follows in general the same pattern as that observed in rabbits (Fig. 15). There are, however, some differences.

The long posterior ciliary arteries are seen as single stems running in the horizontal meridians of the eye. These are usually flanked by short posterior ciliary

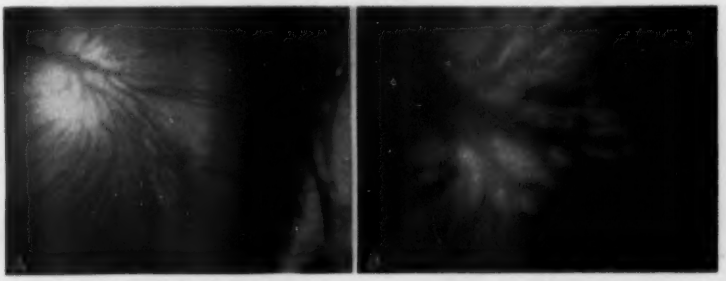


Fig. 17.—Choroidal veins in living guinea pigs. Compare the appearance of these vessels with those in Figure 14. *A*, reduced to 56% of mag. × 10; *B*, reduced to 52% of mag. × 20.

arteries, which have a tortuous course and whose point of origin is not visible in the proptosed eye (Fig. 16). Around these arterial trunks interlaced venules are seen to originate. The venous channels, after following a graceful circular pattern, are directed toward the vortices. In the vortical areas the veins have a radial arrangement; they are less numerous, but more individualized, than in the rabbit (Fig. 17).

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Proteins and Protein Synthesis in Rat Lenses with Galactose Cataract

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It has previously been reported that the accumulation of albuminoid in lenses during the process of aging is associated with an increase in the cystine content of the lens proteins due to its presence in the albuminoid.* Evidence has, furthermore, been brought forward that in rat lenses this accumulation of cystine is due at least partly to an oxidation of cysteine of soluble lens proteins,[1] and it has been pointed out that this oxidative process, which goes on during the life span of the rat, seems to be the result of a delicately balanced equilibrium of oxidative and reductive processes in the lens. This could be necessary for the integration of the albuminoid into the lenticular structure and, therefore, the maintenance of the transparency of the lens. It has long been known [2] that the formation of senile cataract in man is accompanied by an increase of the albuminoid in the lens above the normal level. This finding indicates that an increase in oxidation of lens proteins may play a significant role in the pathogenesis of cataract. A study of this role appears difficult in human cataract because it would require in sufficient number normal human lenses of a well-defined age as controls. It seemed more promising to attempt to elucidate this question by studying changes in the chemistry of lens proteins in various types of experimental cataract. As a first step in this direction, an investigation has been carried out on the galactose cataract of rats.

An increase in the rate of oxidation of lens proteins could be due to one of at least three different factors: (1) an increase in the concentration of oxidizing agents in the lens, (2) an increase in the susceptibility of soluble lens proteins to oxidative agents, or (3) a disturbance of the above-mentioned equilibrium between oxidative and reductive processes due to a disruption of certain structural factors in lens fibers. It appears at present difficult to investigate directly the significance of the first of these three factors, as the oxidation of lens proteins is obviously a very slow process which is difficult to follow under experimental conditions. The susceptibility of lens proteins for oxidation, on the other hand, can be easily investigated, and it can be measured either by the rate of oxidation of sulfhydryl groups of the proteins by certain oxidizing agents or by the amount of such groups available for oxidation. The third factor is obviously very complex. It seems clear, however,

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that one of the elements of this very complex interrelationship of structural factors and metabolic processes could be the continuous synthesis of the insoluble albuminoid and its structural relation to soluble proteins. The rate of this continuous deposition of the insoluble protein has to be a strictly regulated one if the structural integrity of the lens fibers is to be preserved. This rate, at the same time, can be regarded as a measure of the continuous oxidative process taking place in the lens. In experiments here reported, therefore, we compared the rate of formation of soluble proteins and of albuminoid, as well as the behavior of the former toward potassium ferricyanide in lenses of rats of the same age on normal and galactose diets, respectively.

RESULTS

Soluble and Insoluble Proteins in the Lens During Development of Galactose Cataract

To investigate the extent to which an increase in the amount of albuminoid occurs at the expense of soluble proteins in the initial stages of galactose cataract, we determined in a first series of experiments the amount of soluble protein and of albuminoid in the individual rat lens in animals kept on a standard galactose diet, according to the method of Mitchell,[3] as modified by Yudkin and Arnold,[4] for 20 or 21 days and compared these values with those of control animals of exactly the same age, kept on a normal diet during the experimental period. In addition, in one group of animals, the amounts of the two proteins were also determined at the beginning of the experimental period. At that time the age of the animals was 6 weeks. Each group of animals comprised 10 to 16 rats. At the end of the experimental period the two groups of animals were killed with ether; the lenses were removed immediately, dried rapidly with blotting paper, and weighed. Water was then added to each group of lenses corresponding to the tenfold weight of the lenses. The lenses were then crushed as completely as possible with a glass rod and the homogenate centrifuged for one hour at 15,000 rpm in a standard refrigerated centrifuge. The insoluble protein was first washed twice with distilled water, then once with saline, and once with 5% TCA (trichloroacetic acid). The soluble protein was immediately precipitated and the precipitate washed with TCA. The TCA-treated proteins were then hydrolyzed with 6 N HCl, as previously described,[1] and nitrogen determinations were carried out on the hydrolysates. The total protein was then calculated on the basis of 16% nitrogen. The results are listed in Table 1. In Experiments I and II of the Table, after 21 days, all lenses showed marked turbidity. In Experiment III, after 20 days, the turbidity was less pronounced and one-half of the galactose-fed, as well as of the normal, animals were kept for another 12-day period on their respective diets. At the end of this second experimental period six of the galactose animals showed turbidities of about the same degree as the animals in the two other experiments after 21 days, and in three animals a severe cataract developed. The lenses of these two groups were treated separately. As can be seen from Table 1, the lenses of the galactose-fed rats in the first two experiments, characterized by a more rapid development of the cataract, were only about 10% lower in wet weight than those of the control animals. The soluble proteins, however, in the individual lenses were 25% to 30% lower (7 to 7.5 mg., against 10 mg., per lens). The amount of soluble proteins in the galactose-fed animals at 9 weeks was about as great as in normal 6-week-old rats. In Experiment III, in which the development of cataract, at least in some animals, was slower, the wet weight of lenses of galactose-fed animals at the end of the first experimental period was almost exactly the same as that of animals which were killed at the

beginning of the experimental period. That means that there was no significant increase in the volume of the lenses in experimental animals, although in the control group the wet weight increased by about 50%. The soluble protein at the end of the first experimental period in the experimental animals of this series did not increase at all, whereas that in the control group increased by more than 50% (from 6.5 to 10.4 mg.). In the second experimental period of this third experiment the wet weight of both groups of experimental animals, those with the beginning and those with the severer cataract, increased considerably, the first still remaining by about 20%, the second by only 10%, less than the controls. The soluble protein, however, increased only slightly in lenses with initial cataract, and even decreased significantly in lenses with severe cataract.

The insoluble protein presents a very different picture. Here, in all three experiments, the amounts of albuminoid in the experimental animals either did not differ at all, or differed by not more than 20%, from that in the controls. The data indicate, therefore, that the feeding of galactose to rats stops the increase in soluble

TABLE 1.—*Comparison of Amounts of Soluble and Insoluble Proteins in Lenses of Rats of Same Age Fed on Normal and Galactose Diets*

Exper. No.	Diet	No. of Lenses	Wet Wt., Mg./ Lens	Age on Day of Exper. Days	Days After Beginning of Feeding Galactose	Soluble Protein		Insoluble Protein		Ratio Insoluble/ Soluble	Total Protein	
						% Wet Wt.	Mg. per Lens	% Wet Wt.	Mg. per Lens		% Wet Wt.	Mg. per Lens
I	(*a*) Normal	28	32.4	62	21	32.7	10.6	5.9	1.88	0.18	38.0	12.5
	(*b*) Galactose	25	28.8	62	21	27.0	7.8	6.3	1.80	0.22	35.2	9.6
II	(*a*) Normal	22	34.7	62	21	29.4	10.2	10.8	3.3	0.31	40.84	13.4
	(*b*) Galactose	22	30.6	62	21	25.5	7.8	11.4	2.9	0.37	35.0	10.7
III	(*a*) Normal	40	21.0	42	0	34.0	7.1	4.9	1.02	0.14	38.9	8.12
	(*a*) Normal	20	30.0	62	20	34.6	10.4	8.0	2.51	0.24	42.6	12.9
	(*b*) Galactose	20	21.0	62	20	31.5	6.6	9.5	2.0	0.30	41.0	8.6
	(*a*) Normal	18	33.2	74	32	31.5	10.5	10.2	3.38	0.32	41.7	13.9
*	(*b*) Galactose	6	30.0	74	32	18.0	5.4	8.8	2.65	0.49	27.0	8.1
†	(*c*) Galactose	12	25.2	74	32	32.0	8.0	12.5	2.91	0.28	43.2	10.9

* Severe cataract.
† Initial cataract.

protein in the lenses but affects only slightly the accumulation of the insoluble protein. At the same time, there is an increase of the relative amount of water in the lenses in animals on the galactose diet.

OXIDATION OF SOLUBLE PROTEINS AND ITS EFFECT ON THEIR SOLUBILITY IN GALACTOSE-FED RATS

The inhibitory effect of galactose feeding on the rate of the net synthesis of soluble proteins in the lens could come about either by inhibition of protein synthesis or by an increase in protein breakdown. It has been shown in a previous report [1] that lenses of young rats contain, during the period of rapid growth, a protein which becomes insoluble on oxidation with ferricyanide. The amount of this protein decreased with the age, and these changes might be correlated with developmental changes in the pattern of soluble protein and the rate of their synthesis. It was, therefore, to be expected that changes in the synthesis of lens proteins in rats on the galactose diet may also express themselves in the effect of oxidation by ferricyanide on the solubility of protein. We carried out, therefore, a series of experiments in which we determined the availability of reducing groups of soluble lens

proteins for oxidation with ferricyanide and the amount of protein which was precipitated on oxidation. The homogenates of lenses were prepared as described above. The proteins were oxidized with ferricyanide by the procedure previously applied to lens homogenates of rats of various ages.[1] The reduction of the proteins was measured by the amount of ferricyanide reduced after two and a half hours at 38 C. This value was determined by precipitating at the end of this period the experimental sample containing ferricyanide, centrifuging off after two hours' standing in the refrigerator, and comparing the optical density of the TCA filtrate at 420 and 480 mμ with that of a standard solution containing the same amount of ferricyanide as was added to the experimental sample. The difference in D_{420}—D_{480} between the standard and the experimental samples gave the amount of ferricyanide used up by the protein. This value, calculated in micromoles per 100 mg. of protein, are listed in Table 2. It has previously been shown that all available sulfhydryl groups of lens proteins are oxidized under these conditions. The total reduction obtained in this way was the sum of the reduction by the protein and by the

TABLE 2.—*Reduction of $K_3Fe(CN)_6$ and Precipitation of Oxidized Proteins in Lenses of Rats Fed on Normal and Galactose Diets*

Exper. No.		No. of Lenses	Wet Weight, Mg. per Lens	Soluble Protein in Sample	Readings at 480 mμ×1000		μM $K_3Fe(CN)_6$ Reduced per 100 Mg. Protein
					1 Hr.	2 Hr. 30 Min.	
I	Normal	28	22.3	12.2	240	...	10.1
	Cataract	25	28.8	8.3	940	...	12.7
II	Normal	..	34.7	10.3	135	...	10.7
	Cataract	..	30.6	8.1	700	...	11.8
III	Normal	32	29.4	2.26	140	...	6.3
	Cataract	36	28.7	2.24	660	...	7.3
IV	Normal	32	30.3	2.58	45	180	....
	Cataract	32	28.7	2.60	280	595	....
V	Normal	36	28.9	2.60	44	55	....
	Cataract	40	28.0	2.50	61	130	....

TCA-soluble reducing substances, that is, glutathione and ascorbic acid. To obtain the first value, it was necessary to subtract the latter from the total reduction. The reduction of TCA-soluble substances was, therefore, determined on a TCA filtrate of the soluble proteins, which was prepared by precipitation of the solution of soluble proteins with TCA or a control sample at the moment at which ferricyanide was added to the experimental sample. The TCA filtrate of this control sample was neutralized with $NaHCO_3$ and the total reduction of the filtrate was measured with ferricyanide under exactly the same conditions as those of the experimental sample. The reduction by the TCA-soluble substances was only a small fraction of the total reduction. The amount of ferricyanide reduced by the soluble proteins is somewhat larger than corresponds to the amount of oxidized sulfhydryl groups, but the difference is only a small fraction of the total reduction.

The amount of protein precipitated after oxidation was measured by the increase in readings obtained in the Beckman spectrophotometer at 480 mμ with the oxidized protein solution. At this wave length, the optical densities of ferri- as well as of ferrocyanide are negligible, and the readings are a measure of the turbidity of the protein solution due to precipitation. Two series of such experiments were carried out under somewhat different conditions. In the first series, the homogenates of

lenses from experimental and from control animals of the same age were prepared, keeping the ratio of lens weight to suspension fluid identical for the two groups of samples. In a second series (Table 2, Experiments III, IV, V) the concentrations of the protein in solution was considerably lower in experimental than in control samples. In a second series (Table 2, Experiments III, IV, V) the concentrations of protein in solution from control and from experimental animals were very nearly identical. As can be seen from Table 2, the reading at 480 mμ increased with experimental samples in all experiments to a much higher degree than with the corresponding control samples. In one experiment, the protein precipitated from experimental samples was centrifuged off after incubation for two and a half hours at 38 C, and the supernatant, as well as the precipitate after the separation, was treated with 5% TCA, and the amounts of protein in both were determined by nitrogen determination. In this experiment 27% of the total protein of the sample appeared precipitated after oxidation.

In previous experiments on the precipitation after oxidation of soluble proteins from lenses of 5-week-old rats, the percentage of the precipitable protein varied between 22% and 25%. It should, furthermore, be noted that in those experiments in which the concentration of soluble proteins in homogenates from cataractous lenses was the same as in homogenates from normal lenses, the precipitation in the first ones after oxidation caused a much stronger turbidity. All this indicates that the amount of precipitable protein in cataractous lenses from 9-week-old rats is at least equal to, and probably higher than, that in lenses of 6-week-old rats on normal diet.

The ability of soluble lens proteins to reduce ferricyanide was determined in three experiments on protein from cataractous and from normal, control, lenses. The results of these experiments are listed in the last column of Table 2. While the amounts of ferricyanide reduced by 100 mg. of protein were almost identical in Experiments I and II, it was about 40% lower in Experiment III. This was due to the fact that in this last experiment the concentration of proteins was about twice as high as in the two other experiments, and the amount of ferricyanide in the solution dropped very fast, which led to a decrease in the speed of oxidation. In this experiment, therefore, a great part of the reducing group available for oxidation remained unoxidized after two and a half hours at 38 C. In all three experiments, however, the proteins in lenses from rats on the galactose diet reduced 11% to 26% more ferricyanide than did proteins from normal lenses. In Experiments I and II this was not because the homogenates of cataractous lenses contained less protein, as the difference in the concentration of ferricyanide in the solution from cataractous lenses and that in the solution from normal lenses in Experiment I, for example, was less than 6%, and still at the high level. The soluble proteins, therefore, from galactose-fed rats reduced more ferricyanide either because they contained more reducing groups available for oxidation or because the rate of oxidation was enhanced.

COMMENT

The most significant change in lenses of galactose-fed rats, as far as their proteins are concerned, appears to be a strong inhibition of the net synthesis of soluble proteins. This is particularly clear in Experiment III of Table 1. Here, 20 days after the beginning of galactose feeding, the soluble proteins of the lenses showed no significant change. Whereas in rats on normal diet in the same period more

than 3 mg. of soluble proteins was synthesized in every lens, after 32 days in lenses which showed only incipient cataract, no more than 0.9 mg. of lens proteins was formed per lens. In the two other experiments, in which the soluble proteins were not determined at the beginning of the feeding period, an inhibition of the protein synthesis is, nevertheless, clear, as the amounts of soluble protein in lenses of galactose-fed animals are, in both these experiments, 25% below those in lenses of normally fed rats. The wet weight of lenses in Experiment III after 20 days did not differ from that at the beginning of the feeding period; but later on an increase in the water content of the lenses occurred, so that the difference in the wet weights of normal and cataractous lenses became smaller after 32 days than it was after 20 days. The difference in this experiment after 32 days was about the same as, or even greater than, that in the two other experiments after 21 days. It is not clear what is responsible for these variations in the course of the development of cataract in various groups of animals. The fact that in the groups with severe cataract in Experiment III the increase in volume was more marked indicates that this increase in the water content of the cataractous lenses is most probably due to an accumulation of breakdown products of protein. This stage, therefore, of galactose cataract would correspond to the intumescent cataract in humans. Our findings on the effect of the oxidation by ferricyanide on the solubility of lens proteins in the cataractous lens seem to suggest that the decline in the rate of formation of soluble proteins in galactose-fed animals is due rather to an inhibition of synthesis than to an increase in the breakdown.

It has previously been shown that the precipitation of proteins after oxidation with $K_3Fe(CN)_6$ in normal lenses is the more pronounced the younger the animal, and that in 5-week-old animals about three times as much protein is precipitated after two and a half hours at 38 C in per cent of the total protein, and twice as much in absolute terms, as in homogenates from a 10-week-old animal. The pattern of the composition of the soluble-protein fraction of lenses, therefore, changes continuously with the age in the period between 5 and about 20 weeks of life in the same sense as the rate of synthesis of proteins. The continuous decrease in the protein precipitable on oxidation can be best explained by assuming that this protein represents an intermediate stage in the synthesis of the final form of soluble proteins of the lens and that the amount of the first one decreases with the rate of total synthesis. The fact that the galactose-fed rats at the age of 9 weeks contained about as much total soluble protein as, and somewhat more precipitable protein than, they contained at 6 weeks of age, at the beginning of the feeding experiment, means therefore, that galactose feeding arrests the development of the lens as far as the protein pattern is concerned at about the stage at which it is at the start of the galactose feeding. This effect on the intermediary protein could be due either to the inhibition of its transformation into the final form of soluble lens proteins, or to the fact that the decrease in the rate of the protein synthesis with progressing age does not materialize in the galactose-fed animals. Evidence has been brought forth previously which suggests that even during the period of rapid protein synthesis in the lens the net synthesis is the result of a balance between protein formation and protein breakdown.[1] An inhibition of the differentiation of the intermediary protein to the final lens protein would lead first to an accumulation of the first one, which, in turn, might, according to the law of mass action, slow down the formation of the intermediary protein until the over-all synthesis of protein

would be slowed down to the rate of its breakdown, so that no net synthesis would occur any more. This mechanism appears in agreement with the fact that cataractous lenses showed a higher degree of turbidity on oxidation than normal lenses at the time when the galactose feeding started.

If, on the other hand, the higher level of the intermediary protein in cataractous lenses is due to the continuation of the initial rate of protein synthesis during the whole period of galactose feeding, we should have to assume that galactose increases primarily the breakdown of the protein to a level where it balances the total protein synthesis prevailing at the beginning of the experiment. Such an increase in the rate of breakdown of soluble lens proteins could prevent the decline in the rate of protein synthesis with progressing age if the concentration of soluble proteins should be the regulating factor for the rate of protein synthesis. If, owing to a higher breakdown, this concentration remained unchanged during the experimental period, the rate of synthesis would also remain at the same level at which it was at the beginning of the experimental period. Thus, the high level of the precipitable protein would also be explained. In this case, however, there should be no increase in the amount of precipitable protein. Our data, therefore, seem to support the first of the two possible mechanisms of the inhibition of the net synthesis of lens proteins in galactose cataract, but further studies will be necessary to decide this question finally.

The effect of galactose feeding on the formation of the insoluble proteins differs completely from that on soluble proteins. In all three experiments in Table 1, the amount of insoluble protein in the cataractous lenses was either nearly equal (Experiment I) to, or up to 20% lower than, that in normal lenses. It has previously been pointed out that the formation of albuminoid increases with the concentration of soluble protein in the lens, as indicated by the quasi autocatalytic course of the formation of albuminoid in the first five weeks of life. As the amount of soluble proteins in the cataractous lenses is much lower during the feeding period than in normal lenses, a certain decrease in the rate of formation of the albuminoid in the lenses of galactose animals could be expected. If the formation of albuminoid, however, follows the course of a first-degree reaction, this difference would be larger than was actually found. The data from Experiment III indicate, indeed, that the rate of formation of the insoluble protein is greater in galactose-fed rats if we take into account the difference in the concentration of soluble proteins. In this experiment, between 20 and 32 days, as much as 0.9 mg. of albuminoid was formed in the cataractous lenses, that is, as much as in the normal lenses in the same period. This was the case in spite of the fact that at the end of this period the soluble proteins in the cataractous lenses were 25% lower than in the normal ones. The higher rate of the formation of albuminoid appears also in agreement with the fact that the proteins of lenses with galactose cataract reduced more ferricyanide in a certain time than proteins from normal lenses under comparable conditions. Experiments reported in the preceding paper [1] suggest that at least in the young animals albuminoid is formed by oxidation of certain fractions of soluble proteins. In any case, the discrepancy between the effect of galactose feeding on the synthesis of soluble proteins and on that albuminoid leads to a shift in the ratio of these two kinds of proteins in the same sense as is found in senile cataract.

The three changes induced by galactose feeding in the proteins of the lens could take place independently, but it seems more reasonable to assume that they are interdependent. The chain of events could start either with the inhibition of soluble proteins or with the increase in the rate of the breakdown. Evidence was brought

forth previously indicating that in the lens of adult animals synthesis and breakdown of soluble proteins take place simultaneously, and breakdown of soluble proteins, particularly cysteine, is utilized for the synthesis of the albuminoid. It seems reasonable to assume that in the lens of the young rat, between 5 and 10 weeks of age, protein synthesis and proteolysis also proceed simultaneously and amino acids liberated in the second process are utilized in the first one. On this assumption it can be predicted that inhibition of suppression of synthesis or increase in the rate of breakdown of proteins would lead to an accumulation of low molecular products of protein breakdown. The degree of accumulation would depend not only on the rate of the breakdown but on the speed of the diffusion out of the lens. The latter, in turn, would depend on the membrane resistance either on the level of the lens capsule or on the level of the lens fiber surface. Mörner [5] reported as far back as 1894 that the albuminoid is firmly attached to the surface of the lens fibers, whereas the soluble proteins are found in their center, and can be easily removed from there by shaking the lens in water. This fact suggests that the formation of albuminoid, if not accompanied by corresponding stretching of lens fibers, will lead to a thickening of the walls of the fibers and may, indeed, lead to a higher membrane resistance of the surface of the fibers; such a situation seems to prevail in the early stages of the galactose cataract formation, and thus may lead to a decrease in the diffusion of the breakdown products and, consequently, to an increase in the osmotic pressure and to swelling of the lens fibers. Accumulation of protein breakdown products as a causative factor in the intumescent stage of senile cataract has been considered for a long time (Krause [6]).

With the progress of the cataractous process the swelling of the lens continues, but at the same time there appears a very considerable loss of soluble protein. This is shown in Experiment III, where, after 32 days of galactose feeding, those lenses which displayed a dense turbidity even to the naked eye contained no more than 5.2 mg. of soluble protein per lens, as against 7.1 mg. at the beginning of the experiment, but their wet weight was only about 10% less than the wet weight of the normal lenses of the control animals of the same age. The insoluble protein in these lenses was higher than in those cataractous lenses which at the same time did not show as severe cataractous changes.

The question now arises as to the extent to which the changes in proteins of the lens found in the initial stages of the galactose cataract can be considered as pathogenic factors in the cataractous process. The first morphological changes observed in lenses of galactous-fed rats are vacuoles in the cortex of the lens, and it is generally believed that this vacuolation is the expression of a disturbance of the osmotic equilibrium of the lens. The optical transparency of the lens obviously depends on homogeneity of its refractive index. This optical property may depend first on the degree of hydration of lens proteins, as well as on the special interrelation of the different lens proteins, particularly between the soluble proteins and the albuminoid. It seems reasonable to assume that this interrelation between the proteins would produce a certain physicochemical continuity necessary for the optical homogeneity of the lens and that this continuity could be disturbed when the concentration of the soluble proteins drops below a certain minimum. The conditions here may be similar to those in a micellar gel. According to this concept, the optical properties of the lens, therefore, would depend upon a certain ratio between the synthesis of soluble protein and the rate with which it is either oxidized to albumi-

noid or broken down, and any factor which shifts beyond a certain limit the dynamic equilibrium between those two processes will tend to disturb the optical continuity of the lens. If this disruption of the dynamic equilibrium is stronger in certain points, as may be in general expected, vacuolation may result.

Further investigations are now under way to determine whether a mechanism of this kind can be considered as a pathogenetic factor in other forms of cataract in which vacuolation appears to be in the first feasible symptom of the cataractous lenses. The balance between the above-mentioned anabolic and catabolic processes, to which lens proteins are subjected, can be regarded as the result of an adaptation of certain inherited morphogenetic tendencies to specific functional requirements of the lens. These morphogenetic tendencies come from the ectodermal cells, from which the lens epithelium and fibers are derived. These tendencies manifest themselves most distinctly in the keratinization and cornification of the epidermal cells in the vertebrate skin. The keratinization is associated with the replacement of cysteine by cystine, which also takes place during the formation of the albuminoid. A further point of analogy can be seen in the fact that cornification, as well as albuminoid formation, begins on the surface of the cell, and that these two processes with progressing age lead to a depletion of cysteine in the soluble proteins of the epidermis as well as the lens.† It seems possible, furthermore, that the soluble protein in the lens of young animals which accumulates during the period of rapid protein synthesis may be homologous to the protein characterized by the abundance of free sulfhydryl groups which were found to accumulate at the border line between the matrix cells of the epidermal organs and the stratum of cornification.[8] It seems reasonable to assume that the necessity of reconciling the inherited tendency to produce an insoluble protein with the structural requirements imposed by transparency creates a structural stress in the lens which leads to a certain lability of the whole system. Any additional mechanical, nutritional, or metabolic stress exceeding a certain level may in such a case lead to a disturbance which results in the collapse of the structure we observe in the cataractous process.

SUMMARY

Lenses of rats on galactose diet show up to 100% inhibition of the net synthesis of soluble proteins, as compared with controls on normal diet.

This inhibition is accompanied by an accumulation of the protein, which precipitates after oxidation with ferricyanide.

The formation of albuminoid in rat lenses on galactose diet is inhibited no more than 20%.

This inhibition is smaller than could be expected on the assumption that the formation of albuminoid from soluble proteins follows a first-order reaction.

The possible significance of these findings for the pathogenesis of cataract is discussed.

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The Surgical Treatment of Esotropia with Bilateral Depression in Adduction

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In this paper the results of surgery in 65 cases of esotropia with bilateral depression in adduction will be discussed according to the type of procedure done. This group of cases has been defined previously [1] as those in which esotropia is greater for distance and upward gaze than for near and downward gaze, the near point of convergence is good to fair, and a right hypertropia is present on gaze to the right and a left hypertropia on gaze to the left. This group has been termed Group II and the condition is comparable in several respects to esotropia with "divergence insufficiency."

EFFECT OF RESECTION OF ONE LATERAL RECTUS

CASE 1 (B).—A girl aged 15 came to the Infirmary in 1941 with a history of the right eye turning in since 5 years of age. With the perimeter there were 30 degrees of esotropia for distance and 24 degrees for near.

Refraction with atropine cycloplegia was as follows:

O. D.: +1.50 sph=20/20 O. S.: +1.50 sph=20/20

At surgery, on Feb. 13, 1942, a 5 mm. recession of the right medial rectus muscle and a 7 mm. resection of the right lateral rectus muscle was done. The postoperative note one month later stated that the eyes appeared cosmetically straight. The patient returned to the Infirmary in 1952, or 10 years afer surgery, with the following interesting complaint. The appearance of the eyes was satisfactory on gaze straight ahead, but when she danced, being of short stature, she had to look up at her partner and her eyes crossed. The dancing partner would complain that she was looking at someone else instead of at him.

At this time there was 10 degrees of right esotropia in primary position (Fig. 1*A*), 15 degrees of esotropia in supraversion, 15 degrees of exotropia in infraversion, and a good convergence near point. The prism measurements (Fig. 1*A*) were the same for distance and for near but were much greater on looking up than down. A left hypertropia was present but was not greatest in the diagnostic position. No esotropia could be measured in levoversion, while in dextroversion there was an esotropia of 20△. On Aug. 10, 1952, a 10 mm. resection of the left lateral rectus was done. Postoperative examination four months after surgery (Fig. 1*B*) showed that the eyes could be straight for distance and near. On looking up the eyes were straight, but in infraversion there was still 15 degrees of exotropia. The convergence near point was 40 mm., and she fused the four-dot test.

This case presented an interesting surgical problem. How could the esotropia on looking up be corrected without increasing the exotropia on looking down, and possibly causing an exotropia in the primary position? The result of the lateral rectus resection has been gratifying. It has straightened the eyes in the primary position and in supraversion without increasing the exotropia in infraversion. It is to be noted that it has improved the esotropia measurements looking to the right

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ET 18, LH 5

ET'18, LH3

ET20 LH 7	ET16 LH 6	LH12
ET20	ET18 LH 5	LH 6
0	ET 2	LH 8

ET 10	ET 12, LH 4	
ET 2, RH 3	E 2	ET 4, LH 14
XT 2, RH 6	XT 10	XT 14, LH 16

Cover measurements E 4, E' 2
Third grade fusion.

Fig. 1.—*A*, preoperative appearance: (*a*) 5 degrees of right esotropia for near (note Mongoloid slant to palpebral fissures); (*b*) 10 to 15 degrees of right esotropia for distance; (*c*) eyes level on gaze to the right; (*d*) depression of right eye in adduction; (*e*) convergence near point 35 mm.; (*f*) 15 degrees of right esotropia in supraversion; (*g*) 15 degrees of right exotropia in infraversion.

B, postoperative appearance, four months after a 10 mm. resection of the left lateral rectus muscle: (*a*) eyes straight for distance (also for near); (*b*) and (*c*) eyes level on lateral gaze; (*d*) straight in supraversion; (*e*) 15 degrees of right exotropia in infraversion; (*f*) convergence near point 40 mm.

without causing an exotropia looking to the left. The typical vertical deviations were now found postoperatively, viz., a right hypertropia greatest on looking down and to the right and a left hypertropia greatest on gaze down and to the left. The convergence near point has remained 40 mm. This case also demonstrated that the exotropia on looking down, which most likely had been present since the first

TABLE 1.—*Effect of Unilateral Resection of Lateral Rectus Muscle*

Case*	Deviation, Degrees†	Up / Down	NPC, Mm.	Surgery, Mm. Resection	Result, Degrees	Up / Down	Grade of Fusion	P. O. NPC, Mm.	Period Observ., Yr.
A	ET 15	ET 20 / 0	50	8	Straight	ET 10 / 0	I	30	2
B	ET 10	ET 15 / XT 15	50	9	Straight	0 / XT 15	III	60	1
C	ET 10	ET 15 / XT 10	50	9	Straight	0 / XT 10	II	50	1

* All these cases had previous surgery.
† In this Table, and in the accompanying Tables, deviations were estimated by the Hirschberg technique.

operation, 10 years ago, had not affected the convergence near point and did not produce an exotropia for reading or in the primary position.

All the cases in Table 1 had previous surgery with a remaining esotropia in primary position, and all had an esotropia in supraversion. Two cases had an exotropia and one had straight eyes in infraversion. Following a unilateral resection of the lateral rectus muscle all the eyes became straight in the primary position. The resection lessened the esotropia in supraversion and in primary position without increasing the exotropia in infraversion very much, as was illustrated in Case 1. The results were not good in that the eyes were not straight in all positions after operation.

BILATERAL RESECTION OF THE LATERAL RECTI

CASE 2 (D, Table 2).—A child aged 5 years came to the Infirmary in 1951 with a history of the left eye turning in since birth. The left eye would stay in and not move out very well. Refraction with atropine cycloplegia was as follows:

O. D.: +0.25 sph=20/30 O. S.: +0.75 sph=20/20

Examination (Fig. 2*A*) revealed about 25 degrees of esotropia for distance and as little as 15 degrees of esotropia for near at times. About 25 to 35 degrees of esotropia was present on looking up, while the eyes could be straight looking down. Slight depression in adduction was seen on lateral gaze. There was bilateral limitation in abduction. The convergence near point was 15 mm. Cover measurements (Fig. 2*A*) were the same for distance and for near, but were greater on supraversion. A small atypical left hypertropia was found.

At surgery, on July 2, 1952, a bilateral 10 mm. resection of the lateral rectus muscle was done. One year after surgery (Fig. 2*B*) he had about 15 degrees of left esotropia for distance and less esotropia for near. At times the eyes could be straight in the reading position. At a second operation, on May 14, 1953, the left lateral rectus was again resected 5 mm. At examination in August, 1954 (Fig. 2*C*), there was very little improvement in the esotropia.

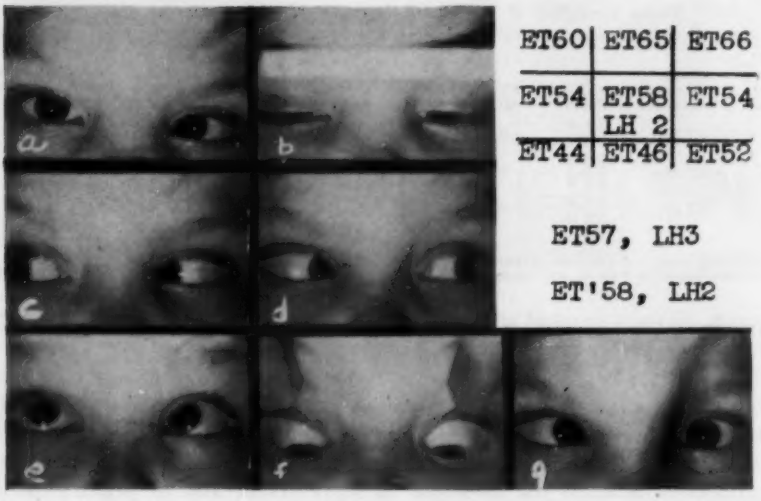
The routine prism cover measurements taken before surgery were not diagnostic except that the esotropia was greater on looking up than down. The cover measurements taken after surgery, including those for the vertical deviations, were typical. The bilateral resection of the lateral rectus muscle, 10 mm. on the right and 15 mm. on the left, failed to correct the esotropia on looking up and in the primary position. The explanation of this failure is not clear but may have been related to paresis of the lateral recti.

CASE 3 (A, Table 2).—A boy aged 3 years came to the Infirmary on Sept. 16, 1948, with a history of occasional crossing of the left eye since one year of age.

Refraction with atropine cycloplegia was as follows:

O. D.: +4.25 sph=20/30 O. S.: +5.25 sph=20/30

He had been wearing his full atropine correction since 1½ years of age, with little improvement in his condition. At examination, on Oct. 22, 1948 (Fig. 3*A*), he had about 25 to 30 degrees of esotropia for both distance and near. However, when he was observed casually in the clinic, his eyes could be very close to straight for near. He was observed for two and a half years,



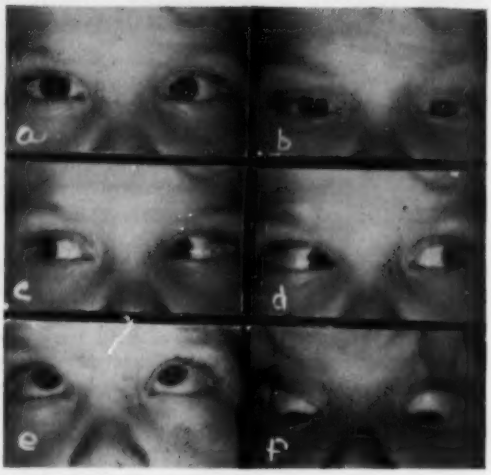
ET60	ET65	ET66
ET54	ET58 LH 2	ET54
ET44	ET46	ET52

ET57, LH3

ET'58, LH2

Fig. 2.—*A*, preoperative appearance: (*a*) 20 degrees of left esotropia for distance; (*b*) about 15 degrees of esotropia in reading position visible clinically; (*c*) and (*d*) slight bilateral depression in adduction with some limitation in abduction noted clinically, but not evident in photographs; (*e*) 20 degrees of left esotropia on looking up; (*f*) eyes straight on looking down; (*g*) NPC 20 mm.

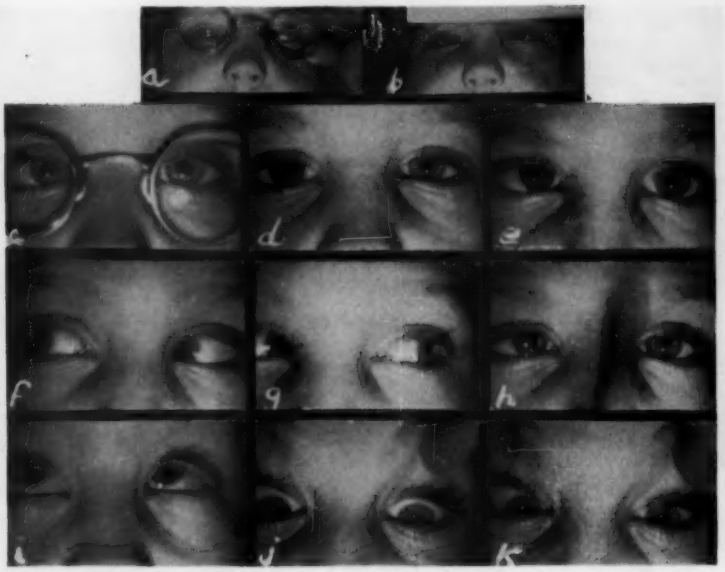
B, postoperative appearance, one year after bilateral 10 mm. resection of lateral rectus muscle: (*a*) 15 to 20 degrees of left esotropia for distance; (*b*) eyes straight in reading position; (*c*) and (*d*) slight bilateral depression in adduction with limitation in abduction noted clinically but not evident in photographs; (*e*) 20 degrees of esotropia in supraversion; (*f*) eyes straight in infraversion.



ET 52	ET 56	ET 58
ET 27, RH 4	ET 33	ET 30, LH 9
RH 12	ET 4	LH 9

Cover measurements ET40, LH3
ET'33, LH8

C, eyes three months after reoperation, consisting of 5 mm. resection of left lateral rectus muscle: (*a*) 10 to 15 degrees of left esotropia for distance; (*b*) 20 degrees of left esotropia in supraversion; (*c*) eyes straight in infraversion.



ET 27	ET 24	ET 22, LH 3
ET 31	ET 26, LH 4	ET 26, LH 5
ET 37	ET 27, LH 5	ET 27, LH 8

cgl ET 22, LH4; ET'17, LH 4
sgl ET 31, LH4; ET'26, LH 4

Fig. 3.—*A*, preoperative photographs, taken in 1948: (*a*) 25 degrees of left esotropia with glasses; (*b*) 20 degrees of left esotropia without glasses.

Preoperative photographs taken April 11, 1951: (*c*) 15 degrees of right esotropia with glasses for near; (*d*) 5 degrees of left esotropia without glasses for near; (*e*) 15 degrees of right esotropia for distance without glasses; (*f*) slight depression of left eye in adduction; (*g*) eyes level on gaze to left; (*h*) near point of convergence, 40 mm.; (*i*) 20 degrees of left esotropia on looking up; (*j*) no deviation on looking down (10 degrees of exotropia at times); (*k*) 5 to 10 degrees of right esotropia on looking down.

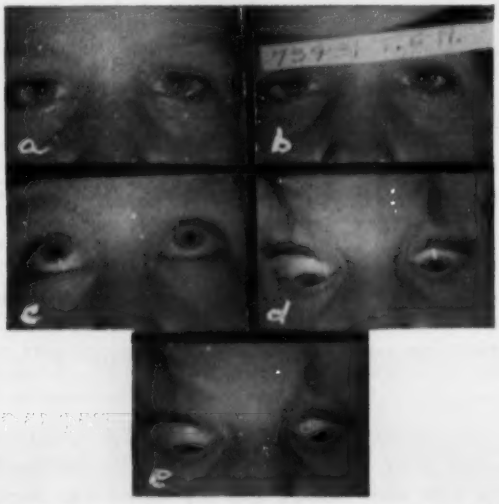
with the hope that the eyes would straighten naturally. Preoperative examination, on April 11, 1951 (Fig. 3*A*), showed that the squint had decreased to about 15 degrees for distance and 5 degrees for near. There was about 20 degrees of esotropia in supraversion and from 10 degrees of esotropia to 10 degrees of exotropia in infraversion.

At surgery, on April 15, 1951, a bilateral 8 mm. resection of the lateral rectus muscle was done. Examination (Fig. 3*B*) two months after surgery revealed that the eyes could be straight for distance and near and in supraversion and infraversion, although most of the time an exotropia was present in infraversion.

At examination three years after surgery (Fig. 3*C*) the eyes were noted to be straight for distance and near without glasses. They were straight in supraversion and diverged about 15 degrees in infraversion most of the time. The convergence near point was 50 mm.

The bilateral resection of the lateral rectus muscle straightened the eyes for distance and upward gaze. The result was excellent, and much better than in Case 2. This may have been because (1) the squint was intermittent, (2) the lateral recti were not paretic, and (3) occasionally prior to surgery a small exotropia was present on looking down.

B, photographs *a* and *b* taken two weeks after surgery; remaining photographs taken two months after surgery: (*a*) 10 degrees of left exotropia with glasses for distance; (*b*) 5 degrees of left exotropia without glasses for distance; (*c*) near point of convergence, 60 mm.; (*d*) 5 to 10 degrees of right esotropia with glasses for distance; eyes straight most of time; (*e*) eyes straight without glasses for near; (*f*) eyes straight looking up; (*g*) and (*h*) eyes level on lateral gaze; (*i*) 10 degrees of left exotropia on looking down; (*j*) eyes straight on looking down.



C, postoperative appearance, three years after surgery: eyes straight (*a*) for distance, (*b*) for near, (*c*) on looking up, (*d*) on infraversion; (*e*) 15 degrees of left exotropia on infraversion.

TABLE 2.—*Effect of Bilateral Resection of Lateral Rectus Muscle*

Case	Deviation, Degrees	Up / Down	NPC, Mm.	Surgery, Mm. Resection	Result, Degrees	Up / Down	Grade of Fusion	Period of Observ., Yr.	NPC, Mm.
A	ET 15	ET 15 / XT 5	25	6/6	Straight	0 / XT 10	I	6	40
B	ET 15	ET 25 / 0	40	10/10	ET 10	ET 20 / 0	II	5	50
C	ET 15	ET 20 / ET 5	25	7/7	ET 18	ET 15 / ET 10	II	1	30
D	ET 25	ET 25 / 0	25	15/10	ET 10	ET 20 / 0	II	4	20
E*	ET 20	ET 35 / XT 5	20	8/8	Straight	ET 25 / XT 25	II	5	40
F	ET 20	N. T.†	25	6/6	ET 5	ET 15 / 0	N. T.	7	35
G	ET 20	ET 25 / ET 5	25	9/9	ET 5	ET 20 / 0	None	2	30
H	ET 20	ET 35 / 0	25	8/8	Straight	0 / 0	III	2	30
I	ET 25	ET 40 / 0	30	7/7	ET 20	ET 25 / XT 5	II	2	30
J	ET 45	ET 50 / ET 35	25	10/10	ET 20	ET 35 / ET 20	II	4	30

* The patient had previous bilateral recession of the medial rectus muscle.
† Not taken.

Table 2 gives the results of the bilateral resection of the lateral rectus muscle in 10 cases. In only three cases did the eyes become straight in the primary position. Of these, two cases had an esotropia looking up and an exotropia looking down before surgery. After operation enough of the esotropia on looking up was diminished and enough of the exotropia on looking down was increased that a balance between these opposite deviations was produced to maintain straight eyes in the central field. Another case, H, had straight eyes in all positions of gaze. This case was unusual, however, in that the patient had an acute onset of what appeared to be a divergence paralysis at the age of 20. He had 20 degrees of esotropia for distance and 35 degrees in supraversion, and he experienced homonymous diplopia. For near and looking down the eyes could be straight; he had no diplopia and had stereopsis. In this case the bilateral resection of the lateral rectus muscle corrected the eyes for distance and upward gaze without disturbing the straight eyes for near and looking down. The remaining seven cases were all undercorrected. All of them had a large esotropia on looking up, with either straight eyes or an esotropia on looking down. The operative procedure did not correct the esotropia on looking up and for distance.

These poor results may indicate that we are dealing with paretic lateral rectus muscles, as in Case 2. It appears that for cases in this group it may be necessary to produce an exotropia on looking down to balance with the esotropia on looking up in order for the eyes to become straight in the central field.

BILATERAL RECESSION OF MEDIAL RECTI

The following two cases had bilateral recessions of the medial rectus muscle.

CASE 4 (E, Table 3).—The child, aged 2 years, came to the Infirmary on April 28, 1949, with a history of the left eye turning in since one year of age.

Refraction with atropine cycloplegia was as follows:

O. D.: +3.75 sph. ⌣ +0.75 cyl, axis 105; O. S.: +3.00 sph. (eccentric fixation)

Following complete occlusion of the right eye, the fixation became centric and steady in the left eye, and eccentric fixation developed in the right eye. This case was one of alternating

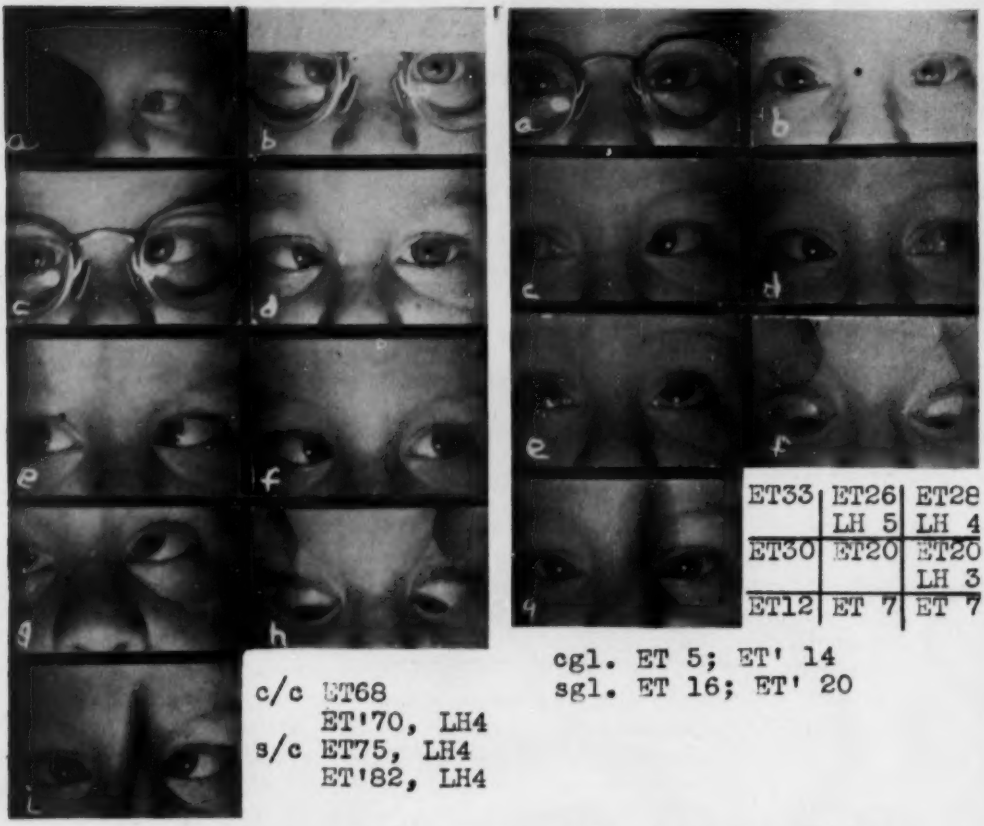


Fig. 4.—*A*, preoperative photographs: (*a*) eccentric fixation of left eye, May, 1949. The remaining pictures were taken on May 10, 1950: (*b*) 35 degrees of right esotropia for distance; (*c*) 25 degrees of left esotropia for near; (*d*) 40 degrees of right esotropia for distance; (*e*) and (*f*) eyes level on lateral gaze; bilateral limitation in abduction; (*g*) 30 degrees of left esotropia in supraversion; (*h*) 20 degrees of left esotropia in infraversion; (*i*) convergence near point 15 mm.

B, postoperative photographs, two years after surgery, in June, 1952: (*a*) eyes straight with glasses for distance and near; (*b*) 5 degrees of left esotropia for distance and near without glasses; (*c*) and (*d*) eyes level on lateral gaze; (*e*) 10 degrees of esotropia in supraversion; (*f*) 10 degrees of exotropia in infraversion; (*g*) convergence near point 25 mm.

amblyopia, and alternating occlusion of the straight eye or the eye with the better vision was instituted for a few hours a day. Preoperative examination (Fig. 4*A*) on May 10, 1950, revealed about 35 to 40 degrees of esotropia for distance and near. Fixation was centric in each eye, and vision in each eye was 20/25. There was 20 to 30 degrees of esotropia in supraversion, about 15 to 20 degrees of esotropia in infraversion, a convergence near point of 15 mm., and limitation of both eyes in abduction.

Surgery on Sept. 14, 1950, consisted of bilateral 5 mm. recession of the medial rectus. At examination two years after surgery (Fig. 4*B*), the eyes were straight with glasses for distance and near, there was about 5 degrees of esotropia without glasses, and the convergence remained very good at 25 mm. There remained 10 to 15 degrees of esotropia in supraversion, and there was about 10 degrees of exotropia in infraversion.

When the patient was seen one month postoperatively, the result of the bilateral recession of the medial rectus muscle was interesting in that the greatest effect was in the straight-down position of gaze; 20 degrees of esotropia was overcorrected to 15 degrees of exotropia, a swing

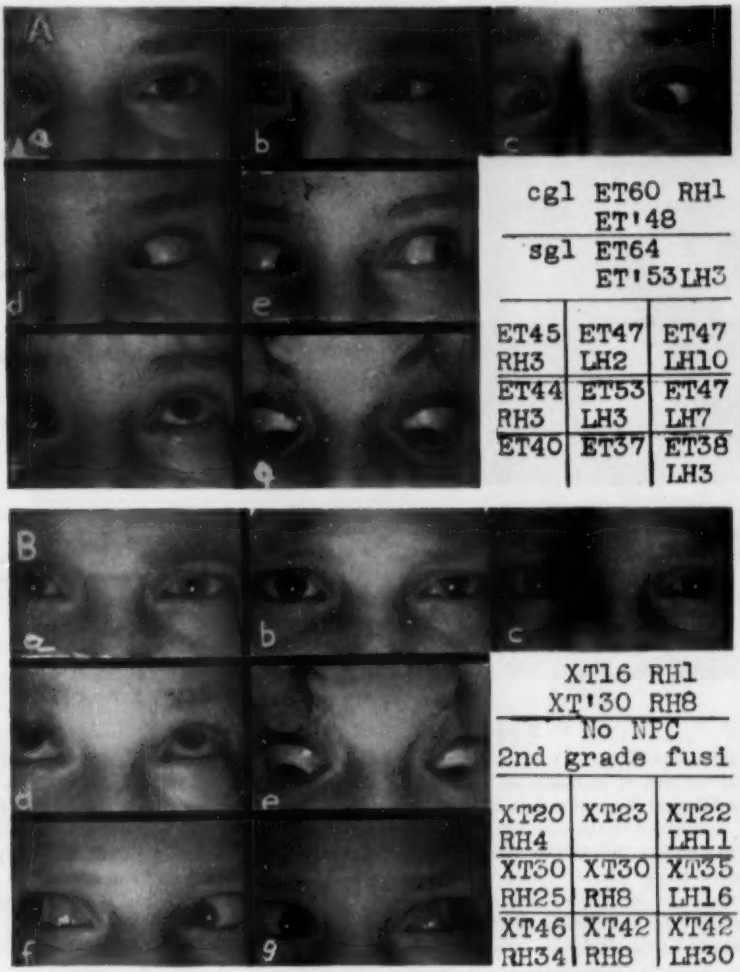
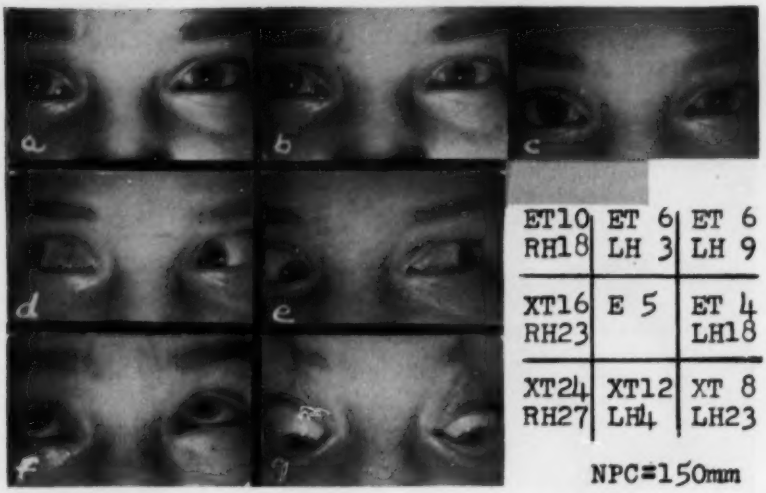


Fig. 5.—*A*, preoperative photographs: (*a*) 20 degrees of right esotropia for near (note Mongoloid slant of palpebral fissures); (*b*) 20 degrees of left esotropia for near; (*c*) convergence near point 25 mm.; (*d*) depression of left eye in adduction; right eye fixing, not visible in photograph; (*e*) depression of right eye in adduction; (*f*) 25 degrees of right esotropia on looking up; (*g*) eyes straight on looking down.

B, postoperative photographs, three months after bilateral 5 mm. recession of medial rectus muscles: (*a*) 5 to 10 degrees of right exotropia for distance; (*b*) 15 degrees of left exotropia for near; (*c*) near point of convergence could not be elicited; (*d*) no deviation on looking up; (*e*) 20 to 30 degrees of right exotropia on looking down; (*f*) depression of left eye in adduction; (*g*) depression of right eye in adduction.

of 35 degrees. On looking up, 30 degrees of esotropia was changed to 20 degrees of esotropia, a swing of 10 degrees. These opposite deviations balanced each other, and the eyes were straight in the central field. Good fusion was present, and what appeared to be a very unstable condition has improved so that at the last examination, in June, 1955, five years after surgery, the eyes have remained straight, with 10 degrees of esotropia on looking up and 10 degrees of exotropia on looking down.

Case 5 (A, Table 3).—A child aged 12 came to the Infirmary on Jan. 12, 1950, with a history of crossed eyes since birth.



C, postoperative photographs, one month after reoperation, consisting of a 4 mm. advancement of right medial rectus and 2 mm. advancement of left medial rectus muscle: (*a*) eyes straight in intermediate position; (*b*) 5 degrees of right exotropia for near; eyes can be straight; (*c*) 5 degrees of right esotropia for distance; eyes can be straight; (*d*) depression of left eye in adduction; (*e*) depression of right eye in adduction; (*f*) 10 degrees of left esotropia on looking up; (*g*) 20 degrees of exotropia on looking down.

Refraction with atropine cycloplegia was as follows:

O. D.: +1.25 sph⌒+1.25 cyl, ax 65=20/30

O. S.: +0.25 sph⌒+1.00 cyl, ax 105=20/30

Examination (Fig. 5*A*) on Feb. 2, 1950, revealed 20 degrees of esotropia for distance and near, 25 degrees of esotropia on looking up, and straight eyes on looking down. There was marked bilateral depression in adduction. The delayed cover test revealed an alternating hypotropia. Horizontal nystagmus was present when both eyes were open and was increased when either eye was occluded. The nystagmus was marked when the eyes were abducted, the quick component being lateral. There were second-grade fusion and normal correspondence with the after-image test. The cover measurements (Fig. 5*A*) were greater for distance than for near and greater on looking up than on looking down. The vertical deviations, however, were not greatest in the diagnostic positions.

Surgery, on May 31, 1950, consisted of a bilateral 5 mm. recession of the medial rectus muscle. The result was a marked overcorrection. Postoperative findings on Aug. 7, 1950 (Fig. 5*B*), were as follows: 5 to 15 degrees of exotropia for distance, 15 to 20 degrees for near, and 30 degrees on looking down, while on looking up the eyes were straight. The delayed cover test revealed an alternating hypertropia instead of an alternating hypotropia, which was present before surgery. No nystagmus could be detected. There was second-grade fusion on the major amblyoscope adjusted for an exotropia of 24 △. The postoperative exotropia did not improve; in fact, it became worse with the passage of time and with convergence exercises.

Reoperation, on Feb. 27, 1951, consisted of a 4 mm. advancement of the right medial rectus and a 2 mm. advancement of the left medial rectus. At operation the muscles were found exactly where they had been placed at the first operation; no slippage had occurred. Postoperative examination on March 24, 1951 (Fig. 5*C*), revealed that the eyes could be straight in the central field. There was 10 degrees of esotropia on looking up and 20 degrees of exotropia on looking down. The delayed cover test was interesting in that no vertical movement was found for near in the central field. When the eyes looked up, about 15 degrees of esotropia and an alternating hypotropia was found. When the eyes looked down, 15 degrees of exotropia and an alternating hypertropia was found.

Following the bilateral recession there was a marked exotropia on looking down, while looking up the eyes were straight. This resulted in an exotropia in the central field, especially for near, which became more marked. It was felt that the medial rectus muscles might have slipped, and so the site of operation was explored. The muscles were found exactly where they had been placed, and were advanced. The change in the relationship between the straight-up and the straight-down position following this procedure was as follows:

The 35 degrees of exotropia on looking down was changed to 20 degrees of exotropia, while on looking up 10 degrees of esotropia developed. With the good fusion ability that was present, a balance between these opposite deviations was possible, and the eyes could be straight in the central fields part of the time, but lapsed into an exotropia much of the time. A larger advancement would seem to have been indicated. The changes in the findings with the delayed cover test are important because they demonstrate that these vertical deviations that were found were innervational, and not paretic. When an esotropia was present before surgery, alternating deorsumduction was present. When an exotropia developed postoperatively, alternating sursumduction was found. After reoperation, when the eyes were straight in the primary position, no vertical deviation was found. On looking up, where an esotropia was present, there was alternating deorsumduction, and on looking down, where an exotropia was present, there was alternating sursumduction.

TABLE 3.—*Effect of Bilateral Recession of Medial Rectus Muscle*

Case	Deviation, Degrees	Up / Down	NPC, Mm.	Surgery, Mm.	Result, Degrees	Up / Down	Grade of Fusion	Period of Observ.	P. O. NPC, Mm.
A	ET 20	ET 25 / 0	25	5/5	XT 15	XT 5 / XT 35	II	8 yr.	200
B	ET 20	ET 35 / XT 15	30	4.5/4.5	XT 20	XT 5 / XT 35	N. T.	3 mo.	50
C*	ET 20	ET 35 / ET 20	20	5/5	Straight	ET 10 / XT 5	II	4 yr.	35
D	ET 20	ET 25 / ET 5	25	3/3	XT 20	XT 5 / XT 35	II	2 yr.	50
E	ET 25	ET 25 / ET 20	25	5/5	Straight	ET 15 / XT 15	II	5 yr.	40
F†	ET 35	ET 45 / ET 35	40	5/5	ET 20	ET 35 / XT 5	II	5 yr.	50

* Patient had a bilateral resection of the lateral rectus muscles previously.

† Reoperation later; a bilateral resection of the lateral rectus muscle was done later (shown in Table 2, Case E).

Table 3 gives the results of the bilateral recession of the medial rectus muscle in six cases. In two cases the eyes became straight after surgery; three cases had overcorrection, and one case had undercorrection. The preoperative findings of the straight cases were compared with those of the overcorrected cases to see if any reason could be found for the overcorrection. Before surgery all had at least 20 degrees of esotropia in the primary position, with a good near point of convergence and at least 25 degrees of esotropia on looking up. The only significant difference was in the amount of esotropia on looking down. The straight cases had at least 20 degrees of esotropia on looking down, while of the overcorrected cases one had straight eyes, one had 5 degrees of esotropia, and one had 15 degrees of exotropia on looking down. After surgery in the cases in which the eyes became straight the large esotropia on looking down was overcorrected to a small exotropia in this position. This balanced with a small, remaining esotropia on looking up. In the overcorrected cases there developed a large exotropia of at least 35 degrees on looking down. A small exotropia developed on looking up, and the result was an exotropia in the primary position. From these preoperative findings and results of surgery, it appeared that the bilateral recession of the medial rectus muscle had a large effect on the deviation present in downward gaze. The overcorrected cases had

insufficient esotropia on looking down for the amount of recession done. The undercorrected case also showed the effect of the bilateral recession in the downward position of gaze. In this case there was at least 35 degrees of esotropia in the primary position, with 45 degrees on looking up and 35 degrees on looking down. The bilateral recession corrected the 35 degrees of esotropia on looking down, while at least 35 degrees of esotropia remained on looking up. This resulted in 20 degrees of esotropia remaining in the primary position. At reoperation a bilateral resection of the lateral rectus muscle was done (Table 2). Following this the eyes became straight in the primary position, but now 25 degrees of exotropia was seen on looking down, which balanced with 25 degrees of esotropia remaining on looking up.

RECESSION OF MEDIAL RECTUS AND RESECTION OF LATERAL RECTUS OF ONE EYE

In the following two cases a unilateral recession of the medial rectus and a unilateral resection of the lateral rectus muscle was done at operation.

CASE 6 (C, Table 4).—The patient, aged 13 years, came to the Infirmary in April, 1948, with a history of the eyes crossing since birth. Refraction with atropine cycloplegia was as follows:

O. D.: +0.25 cyl, ax 90=20/20

O. S.: +0.25 cyl, ax 90=20/20

Examination revealed (Fig. 6*A*) 30 degrees of esotropia for distance, 25 degrees for near, 25 degrees on supraversion, and straight eyes on infraversion. With the delayed cover test alternating sursumduction was found. The patient had a Mongoloid slant to the palpebral fissures.

At surgery, on May 4, 1948, a 5 mm. recession of the right medial rectus muscle and a 9 mm. resection of the right lateral rectus muscle was done. Postoperative examination (Fig. 6*B*) in August, 1951, three years after the operation, revealed straight eyes for distance and near and on supraversion. There was 20 degrees of exotropia on infraversion. Second-grade fusion was present at 0 on the troposcope. The prism-cover measurements showed a small remaining esophoria for distance and near. In supraversion there was a small esotropia, and in infraversion, a small exotropia. In dextroversion there was an esotropia; in levoversion, an exotropia.

This case demonstrated the ability of eyes with good fusion to adjust themselves in order to remain straight in the central field of gaze. A balance was effected not only between an esotropia looking up and an exotropia looking down, but also between an exotropia in levoversion and an esotropia in dextroversion (see cover measurements in Fig. 6*B*).

CASE 7 (G, Table 4).—A girl aged 5 came to the Infirmary on Aug. 14, 1947, with a history of the left eye turning in since 6 months of age. Examination (Fig. 7*A*) revealed, without glasses, 25 degrees of esotropia for distance and 20 degrees for near; with glasses, 10 degrees of esotropia for distance and 15 degrees for near. There was about 40 degrees of esotropia in supraversion and 15 degrees in infraversion. The eyes were level on lateral gaze. The convergence near point was 25 mm.

Refraction with atropine cycloplegia was as follows:

O. D.: +4.00 sph⁀+0.50 cyl, ax 90=20/20

O. S.: +4.25 sph⁀+0.50 cyl, ax 90=20/20

She had second-grade fusion and normal retinal correspondence. Prism-cover measurements (Fig. 7*A*) were the same for distance and near and were greater on looking up than on looking down. Glasses reduced the deviation more for distance than for near.

At surgery, on Nov. 13, 1948, a 4 mm. recession of the left medial rectus muscle and an 8 mm. resection of the left lateral rectus muscle was done. Postoperative examination on June 10, 1949 (Fig. 7*B*), revealed 10 degrees of exotropia with glasses for both distance and near. Without glasses the eyes were straight. In supraversion the eyes were straight, and in

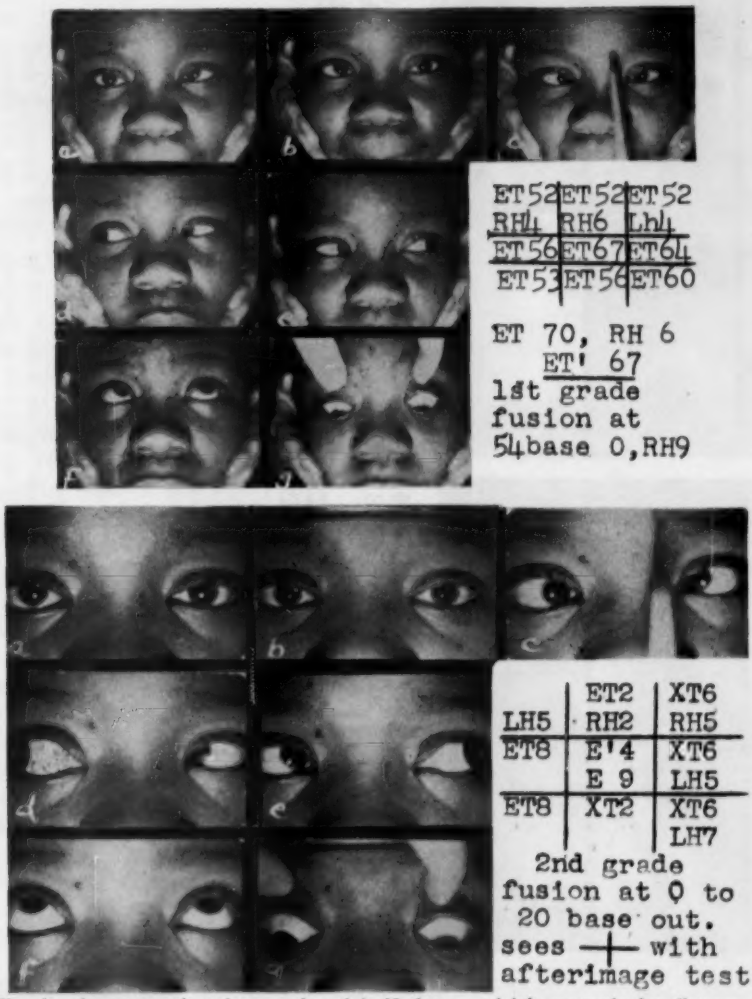


Fig. 6.—*A*, preoperative photographs: (*a*) 30 degrees of left esotropia for distance (note Mongoloid slant to palpebral fissure); (*b*) 25 degrees of right esotropia for near; (*c*) near point of convergence 20 mm.; (*d*) eyes level on gaze to right; (*e*) slight depression of right eye in adduction; (*f*) 25 degrees of right esotropia on looking up; (*g*) eyes straight looking down.

B, examination July, 1950, two years after surgery, which consisted of 5 mm. recession of right medial rectus and 9 mm. resection of right lateral rectus muscle: (*a*) eyes straight for distance; (*b*) eyes straight for near; (*c*) near point of convergence 25 mm.; (*d*) and (*e*) eyes appear level on lateral gaze; bilateral depression in adduction seen well clinically; (*f*) eyes straight looking up; (*g*) 20 degrees of right exotropia on looking down.

infraversion there was 25 degrees of exotropia. The convergence near point was 50 mm. Prism-cover measurements were as follows:

With glasses	XT 4; XT' 4	In supraversion ET 2
Without glasses	X 2; E' 2	In infraversion XT 6

The child was told not to wear her glasses for one month and to return to the clinic.

When she was next examined, on July 10, 1949, the findings had changed radically (Fig. 7*C*). Without glasses she had about 15 degrees of esotropia for distance and 10 degrees for near. Bilateral depression in adduction was easily seen. The convergence near point was

Fig. 7.—*A*, preoperative photographs: (*a*) 25 degrees of left esotropia for distance without glasses; (*b*) 10 to 15 degrees of esotropia with glasses; (*c*) and (*d*) eyes level on lateral gaze; (*e*) 35 degrees of esotropia in supraversion; (*f*) 10 to 15 degrees of esotropia in infraversion; (*g*) convergence near point 25 mm.

B, postoperative appearance, seven months after 4 mm. recession of left medial rectus and 8 mm. resection of left lateral rectus muscles: (*a*) eyes straight for distance and near without glasses; (*b*) 10 degrees of exotropia for distance and near with glasses; (*c*) and (*d*) slight depression in adduction bilaterally; (*e*) eyes straight in supraversion; (*f*) 25 degrees of exotropia in infraversion; (*g*) convergence near point is 50 mm.

C, appearance after going without glasses for one month: (*a*) 15 to 20 degrees of right esotropia for distance; (*b*) 10 to 15 degrees of right esotropia for near; (*c*) and (*d*) bilateral depression in adduction; (*e*) 25 degrees of esotropia in sursumversion; (*f*) 5 degrees of exotropia in infraversion; eyes can also be straight; (*g*) convergence near point 30 mm.

D, three months after wearing a reduced correction: (*a*) eyes straight for distance and near with glasses; (*b*) 10 degrees of left esotropia for distance and near without glasses; (*c*) 10 degrees of esotropia in supraversion; (*d*) 10 degrees of exotropia in infraversion.

30 mm. In supraversion there was 25 degrees of esotropia; in infraversion the eyes could be straight. Prism-cover measurements were as follows:

Without glasses ET 30; ET' 20

The lenses were reduced to the following correction:

O. D.: +2.00 sph⌒+0.75 cyl, ax 90=20/20
O. S.: +2.75 sph⌒+0.75 cyl, ax 90=20/20

This correction was to be worn all the time. After it had been worn for three months, the eyes became straight with glasses for distance and near (Fig. 7*D*), and now 10 degrees of esotropia was present on looking up and 10 degrees of exotropia on looking down.

In this patient the changes in the relationship of the straight-up and the straight-down positions of gaze can be seen to be dependent on the kind and amount of squint present in primary position. After surgery, with glasses there was an exotropia of 10 degrees (Fig. 7*B*), with 25 degrees of exotropia on looking down and straight eyes on looking up. After the glasses had not been worn for one month (Fig. 7*C*), an esotropia of 15 to 20 degrees developed again, and there was then 25 degrees of esotropia on looking up and only 5 degrees of exotropia on looking down. Then a reduced plus correction was given and the eyes became straight with glasses for distance and near (Fig. 7*D*), and now there was a balance between 10 degrees of esotropia on looking up and 10 degrees of exotropia on looking down.

The results of the recession of a medial rectus and the resection of a lateral rectus muscle at the same time in 37 cases are given in Table 4. After surgery the eyes were straight in the primary position in 26 cases. However, in none of these cases were the eyes straight in all positions. In 15 cases an esotropia remained on looking up and an exotropia was found on looking down. In six cases the eyes appeared straight on looking up with the Hirschberg test, although a small esotropia was measured with the cover test. In looking down an exotropia was present. Of the remaining five cases with straight eyes, four had a small esotropia on looking up, with straight eyes on looking down, and one was not examined in these positions. Eight cases were undercorrected, and all of these had a remaining esotropia on looking up. Of these eight cases, six had straight eyes on looking down; one had a large esotropia on looking down, and one had an exotropia on looking down (Case C'). Five of these undercorrected cases had more than 25 degrees of esotropia before surgery, indicating that this amount of squint was difficult to correct by operation on only two muscles. Three cases were overcorrected, and of these, two developed a large exotropia on looking down and a small exotropia on looking up, and one had a large exotropia on looking down, with straight eyes on looking up. From the results following the unilateral recession and resection operation, it appeared that cases in which there developed an exotropia on looking down with an esotropia remaining on looking up had the best chance of getting straight eyes in the primary position.

RECESSION OF BOTH MEDIAL RECTI AND RESECTION OF ONE LATERAL RECTUS

In the following case a bilateral medial rectus recession and a left lateral rectus muscle resection was done.

CASE 8 (D, Table 5).—A child aged 6 years came to the Infirmary on March 15, 1948, with a history of crossed eyes since birth. Refraction with atropine cycloplegia was as follows:

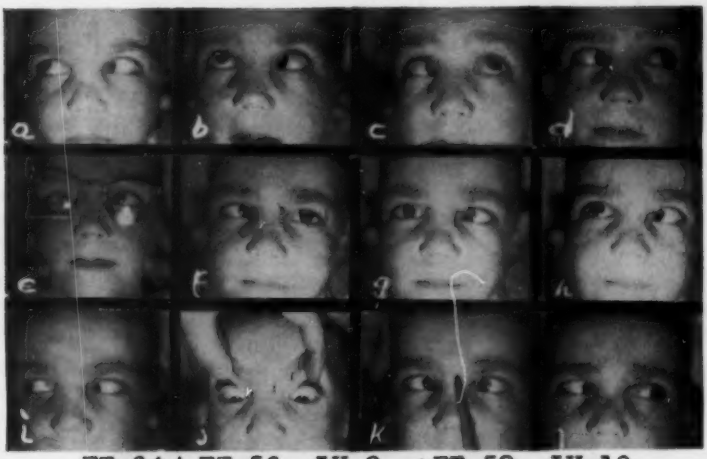
O. D.: +4.25 sph=20/20
O. S.: +5.00 sph=20/70

With complete occlusion of the right eye, vision in the left was brought up to 20/30. Wearing the full atropine correction did not seem to affect the esotropia very much. Examination findings on June 15 (Fig. 8*A*) revealed 40 degrees of esotropia on looking up and 15 degrees

TABLE 4.—*Effect of Unilateral Recession of Medial Rectus Muscle and Unilateral Resection of Lateral Rectus*

Case	Deviation, Degrees	Up / Down	NPC, Mm.	Surgery, Mm.	Result, Degrees	Up / Down	Grade of Fusion	NPC, Mm.	Period Observ.
A	ET 10	ET 10 / 0	30	4/7	Straight	0 / XT 15	II	40	2 yr.
B	ET 15	ET 15 / 0	35	4/7	Straight	0 / XT 15	II	40	2 yr.
C	ET 15	N. T.	30	5/5	Straight	0 / XT 15	None	200	8 yr.
D	ET 15	ET 20 / ET 5	30	5/6	ET 10	ET 15 / 0	II	40	3 yr.
E	ET 20	ET 20 / 0	35	5/8	Straight	ET 10 / XT 5	N. T.*	40	3 mo.
F	ET 20	ET 20 / ET 25	50	4/6	Straight	0 / XT 15	II	100	1 yr.
G	ET 20	ET 25 / ET 10	25	4/8	Straight	ET 10 / XT 10	II	40	5 yr.
H	ET 20	ET 25 / ET 20	40	5/10	Straight	ET 15 / XT 5	II	100	2 yr.
I	ET 20	ET 30 / ET 20	30	4/8	ET 10	ET 20 / 0	II	30	6 yr.
J	ET 20	N. T.	30	5/8	Straight	ET 10 / 0	None	50	6 yr.
K	ET 20	ET 45 / ET 35	30	5/8	Straight	ET 10 / XT 5	II	35	3 yr.
L	ET 20	ET 30 / ET 20	30	3/8	Straight	ET 15 / XT 10	II	50	4 yr.
M	ET 20	ET 20 / ET 5	70	5/8	Straight	ET 15 / 0	II	50	3 yr.
N	ET 20	ET 25 / ET 20	35	5/7	Straight	ET 10 / 0	II	40	2 mo.
O	ET 15	N. T.	50	5/8	XT 10	XT 5 / XT 15	II	50	3 yr.
P	ET 20	N. T.	50	5/8	ET 5	ET 15 / 0	II	90	2 yr.
Q	ET 20	ET 30 / ET 10	60	5/6	Straight	0 / XT 20	I	140	7 yr.
R	ET 20	ET 35 / ET 20	30	5/8	XT 5	XT 5 / XT 15	II	55	3 yr.
S	ET 20	N. T.	35	5/8	Straight	N. T.	II	40	1 yr.
T	ET 20	ET 25 / ET 15	30	4/7	Straight	ET 10 / XT 15	II	35	5 yr.
U	ET 20	ET 25 / ET 10	25	4/8	Straight	ET 10 / XT 10	II	35	6 yr.
V	ET 20	N. T.	25	5/8	Straight	ET 5 / XT 5	II	75	7 yr.
W	ET 20	ET 25 / ET 5	25	5/9	XT 5	0 / XT 25	None	150	1½ yr.
X	ET 20	ET 20 / 0	25	5/9	Straight	0 / XT 20	II	20	3 yr.
Y	ET 20	ET 25 / ET 10	25	5/8	Straight	ET 20 / XT 20	II	40	3 yr.
Z	ET 20	ET 20 / ET 10	50	5/8	Straight	ET 5 / XT 20	II	200	5 yr.
A'	ET 20	ET 35 / ET 25	25	4/10	Straight	ET 10 / XT 10	II	40	2 yr.
B'	ET 25	ET 45 / ET 25	..	5/8	Straight	ET 15 / 0	None	50	1 yr.
C'	ET 25	N. T.	35	5/7	ET 10	ET 15 / XT 15	I	50	10 yr.
D'	ET 25	ET 35 / ET 15	35	5/8	Straight	ET 15 / XT 10	III	40	1 yr.
E'	ET 25	ET 35 / ET 10	30	5/9	Straight	ET 10 / XT 10	III	30	4 yr.
F'	ET 25	ET 35 / ET 25	25	5/10	Straight	ET 15 / XT 15	III	30	5 yr.
G'	ET 35	N. T.	30	5/9	ET 15	ET 20 / 0	I	35	4 yr.
H'	ET 35	ET 40 / ET 25	45	4/9	Straight	ET 15 / XT 10	II	200	8 yr.
I'	ET 35	ET 45 / ET 40	40	5/8	ET 10	ET 20 / 0	II	75	8 yr.
J'	ET 40	N. T.	50	5/7	ET 20	ET 25 / 0	N. T.	50	1 yr.
K'	ET 40	N. T.	15	5/7	ET 20	ET 30 / ET 20	N. T.	30	4 yr.

* Not taken.



ET 64	ET 56, LH 8	ET 52, IH 10
ET 58	ET 45, LH 10	ET 52, LH 10
ET 60	ET 48, LH 10	ET 54, LH 8

Cover Measurements: cgl. ET 50, LH 13; ET'45, LH 10
sgl. ET 58, LH 13; ET'45, LH 10

ET34	ET30, LH10	ET25, LH12
E 16, LH3	E 16, LH18	E 7, LH18
XT15, RH4	E 18, LH12	E 6, LH24

Cover measurements: cgl E 14, LH15; E'10, LH14
sgl. ET20, LH16; E 16, LH18.

NPC = 35mm.
2nd gr. fusion
at RH2 on Tropo.

Fig. 8.—*A*, preoperative photographs: (*a*) limitation of left eye up and to right; (*b*) 40 degrees of left esotropia looking up with marked limitation in elevation of left eye; (*c*) 40 degrees of right esotropia looking up with marked limitation in elevation of right eye; (*d*) limitation of right eye up and to left; (*e*) 25 degrees of left esotropia for near with glasses; (*f*) 30 degrees of right esotropia for near without glasses; (*g*) 40 degrees of left esotropia for distance; (*h*) 45 degrees of left esotropia for distance; (*i*) depression of left eye in adduction; (*j*) eyes straight looking down; 15 degrees of esotropia looking down most of time; (*k*) near point of convergence 15 mm.; (*l*) eyes level on gaze to left; depression in adduction seen clinically.

B, postoperative appearance, two years after bilateral 3.5 mm. recession of medial rectus muscles and an 8 mm. resection of left lateral rectus muscle: (*a*) eyes straight with glasses for distance; (*b*) eyes straight without glasses for near; stereopsis at 0; (*c*) 5 to 10 degrees of left esotropia for distance without glasses; (*d*) eyes level on dextroversion; (*e*) eyes level on levoversion; (*f*) good elevation of left eye up and to right (compare with *A*, *a*). (*g*) 10 degrees of left esotropia looking up; good elevation of left eye (compare with *A*, *b*); (*h*) 5 degrees of left exotropia on looking down; (*i*) good elevation of right eye up and to left (compare with *A*, *d*).

ET40	ET34, LH9	ET20, LH16
ET14, LH1	E'4	ET19, LH12
0	ET 8, LH9	ET6, LH12

s/c ET20, LH14; ET'18, LH12
c/c E 6, LH8: E'4, LH5

C, six years postoperatively, Oct. 28, 1954: (*a*) eyes straight with glasses; (*b*) eyes straight without glasses; (*c*) and (*d*) obliques elevate the eyes well; (*e*) convergence near point 30 mm.; (*f*) 10 degrees of esotropia in supraversion; (*g*) 15 degrees of right exotropia in infraversion; (*h*) eyes straight on infraversion.

of esotropia on looking down, and about 40 degrees for distance and 30 degrees for near. Bilateral depression in adduction was present; the near point of convergence was 15 mm. The delayed cover test revealed alternating sursumduction, bilateral wheel rotation in, and occlusion nystagmus. The limitation of the adducted eye in straight-up (Fig. 8*A*, *b*, *c*) and in the oblique positions (*a*, *d*) was so marked that a diagnosis of bilateral inferior oblique paralysis was made. The bilaterality of the condition could be seen clearly on versions; yet the cover measurements showed only a left hypertropia, not greatest in the diagnostic position. The depression in adduction was much more pronounced on gaze to the right; yet no hypertropia was found in this position. The finding of only a left hypertropia with cover measurements was due most likely to the previous amblyopia of the left eye (dissociated left hypertropia).

Examination on Oct. 10, 1951 (Fig. 8*B*), three years after surgery, revealed the eyes to be straight for distance and for near. There were 10 degrees of esotropia on looking up and 5 degrees of exotropia on looking down. Cover measurements (Fig. 8*B*) showed a greater esotropia for distance than for near without glasses and only a phoria with glasses. Bilateral vertical deviations were found greatest in the typical positions. The findings with the delayed cover test were very interesting and showed the variability of the innervational vertical and rotary deviations. Most of the time the left eye was up under cover, while the right eye remained horizontal under cover. Bilateral wheel rotation in could be seen at times. At other times the left eye would be up under cover, and wheel rotation in was seen when it came down to fix. The right eye would be down under cover and display wheel rotation out when it came

up to fix. The horizontal muscle surgery improved the apparent bilateral paralysis of the inferior obliques (Fig. 8*B*, *d*, *e*, *f*, *g*, and *i*), demonstrating that this apparent limitation in movement of the oblique muscles was secondary to the horizontal squint, and not a primary paresis of the inferior obliques.

Examination six years after surgery (Fig. 8*C*) showed a definite improvement in the vertical cover measurements, especially with glasses. Only a left hypertropia was found at this time, not greatest in the diagnostic position. With the troposcope the patient had third-grade fusion at 0, with no hypertropia adjustment.

Straightening the eyes with horizontal muscle surgery cured what appeared to be an almost complete paralysis of the inferior oblique muscles. With the delayed cover test, before surgery alternating sursumduction with alternating incycloduction was found, while after surgery variations were found as follows: At times there was only a left hypertropia with incycloduction, and at other times a right hypotropia with excycloduction.

TABLE 5.—*Effect of Bilateral Recession of Medial Rectus Muscle and Unilateral Resection of the Lateral Rectus*

Case	Deviation, Degrees	Up / Down	NPC, Mm.	Surgery, Mm.	Result, Degrees	Up / Down	Grade of Fusion	Period Observ.	P. O. NPC, Mm.
A	ET 40	N. T.*	70	4/4/8	XT 10	N. T.	N. T.	7 mo.	N. T.
B	ET 40	N. T.	60	4/4/8	XT 15	XT 5 / XT 20	N. T.	1 yr.	60
C	ET 35	N. T.	25	3/3/8	Straight	ET 20 / XT 10	III	5 yr.	25
D	ET 35	ET 45 / ET 15	25	3/3/8	Straight	ET 10 / XT 15	III	7 yr.	30
E	ET 30	ET 50 / ET 15	25	3/3/8	Straight	ET 20 / XT 10	III	6 yr.	50
F	ET 35	N. T.	25	4/4/10	Straight	0 / XT 20	I	1 yr.	60
G	ET 35	N. T.	25	4/6/8	XT 10	N. T.	II	6 mo.	N. T.
H	ET 35	N. T.	30	4/4/8	Straight	ET 20 / XT 10	II	6 yr.	45
I	ET 35	N. T.	25	3/3/8	Straight	ET 15 / XT 10	II	1 yr.	50

* Not taken.

With prism-cover measurements, before surgery only a left hypotropia was found, while three years postoperatively bilateral hypertropias were found, which were greatest in the diagnostic positions. Even though a large hypertropia was present in the primary position, third-grade fusion at 0 on the troposcope was elicited. With the straightening of the eyes the occlusion nystagmus, although still present, became less marked. All these variations in the above findings indicate that they are innervational and dissociated phenomena, due to the disruption of fusion by the horizontal squint, and not paretic in origin.

Table 5 gives the results of a bilateral recession of the medial rectus and a unilateral resection of a lateral rectus muscle done at the same operation in the nine cases in which it was done. All these cases had an esotropia before surgery of 35 degrees or more, and it was felt that operation on only two muscles would not be sufficient. It was interesting to note that three cases had an overcorrection and there were none that had an undercorrection. Six cases obtained straight eyes in the primary position, and all but one case had an esotropia on looking up and an exotropia on looking down after operation. The convergence near point remained good in these cases.

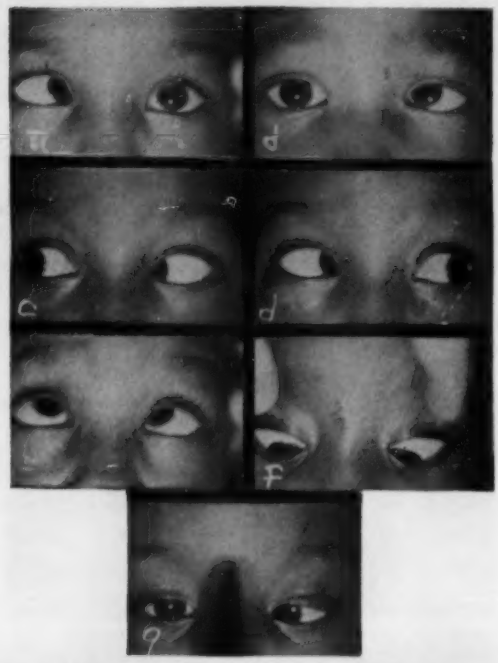


Fig. 9.—*A*, preoperative photographs: (*a*) 45 degrees of right esotropia for distance; (*b*) 35 degrees of left esotropia for near; (*c*) and (*d*) eyes level on lateral gaze; (*e*) 35 degrees of esotropia in sursumversion; (*f*) 20 degrees of esotropia in infraversion; (*g*) convergence near point 15 mm.

B, postoperative photographs: (*a*) 10 degrees of left esotropia for distance; (*b*) eyes can be straight for near when reading without glasses; (*c*) eyes can be straight for near with glasses; (*d*) and (*e*) eyes level on lateral gaze, better movement in abduction; (*f*) 15 degrees of esotropia in supraversion; (*g*) 5 to 10 degrees of exotropia in infraversion.

RESECTION OF BOTH LATERAL RECTI AND RECESSION OF ONE MEDIAL RECTUS

CASE 9 (B, Table 6).—A child aged 3½ years came to the Infirmary on June 4, 1952, with a history of crossed eyes since about 3 months of age. Refraction with atropine cycloplegia was as follows:

O. D.: +2.00 sph=20/50

O. S.: +2.50 sph=20/30

Glasses had little effect on the esotropia. About 45 degrees of esotropia could be present for distance (Fig. 9*A*) and about 35 degrees for near. In supraversion there was 35 degrees of esotropia, and in infraversion, 20 degrees. The convergence near point was 15 mm.

At surgery, in September, 1952, the patient had a bilateral 8 mm. resection of the lateral rectus and a 4 mm. recession of the left medial rectus muscle. Postoperative examination nine months after surgery (Fig. 9*B*) revealed 10 degrees of esotropia remaining for distance and near, although the eyes could be straight for near in the reading position. About 15 degrees of esotropia remained in supraversion, while in infraversion the deviation varied from 0 to 15 degrees of exotropia. The convergence near point was 40 mm. A right hypertropia, greatest on gaze up and to the right, in the diagnostic position, was present.

For such a large esotropia of 45 degrees the cosmetic result after surgery was excellent. Perhaps a larger recession of the medial rectus muscle should have been done. This would have increased the exotropia in looking down to balance with the remaining esotropia in looking up, for straighter eyes in the primary position.

TABLE 6.—*Effect of Bilateral Resection of Lateral Rectus Muscle and Unilateral Recession of Medial Rectus Muscle*

Case	Deviation, Degrees	Up / Down	NPC, Mm.	Surgery, Mm.	Result, Degrees	Up / Down	Grade of Fusion	P. O. NPC, Mm.	Period Observ. Yr.
A	ET 35	ET 45 / ET 20	30	10/10/4	Straight	0 / 0	II	30	5
B	ET 40	ET 45 / ET 20	20	8/8/4	ET 5	ET 15 / XT 10	I	50	1
C	ET 25	ET 30 / 0	50	10/10/4	ET 15	ET 15 / XT 5	II	80	1

Three cases (Table 6) had a bilateral resection of the lateral rectus muscles and a unilateral recession of a medial rectus muscle. These cases all had at least 25 degrees of esotropia before surgery. Postoperatively in one case the eyes became straight in all positions, a rather rare result for this group. In the two cases with undercorrection there remained a larger esotropia on looking up than the exotropia on looking down. A larger recession would seem to have been indicated to increase the exotropia on looking down in order to achieve a better balance in the primary position.

COMMENT

The cases presented in this paper emphasize the value of noting the up and down positions of gaze in examination of esotropia, because of their importance in deciding which muscles are to be attacked surgically. From the data in Table 7, the average reduction in the amount of esotropia on looking up was greater after a resection of one or both lateral recti muscles than the reduction in the amount of esotropia on downward gaze. On the other hand, recession of one or both medial recti produces a relatively greater effect on the downward gaze. The exceptions to these general principles are also given in Table 7. The actual amount of correction obtained following a recession of the medial rectus is greater than a corresponding resection of the lateral rectus, even for the amount of esotropia present on upward gaze. This is in general accord with the well-known fact that more correction is

obtained by recessions than by resections. Accordingly, for those cases of esotropia with relatively little deviation, mostly present on upward gaze, resection of one or both lateral recti might well be considered. Larger amounts of esotropia require recessions of one or both medial recti, which should be done conservatively if the esotropia on downward gaze is relatively small.

Following surgery, the majority of cases that obtained straight eyes in the primary position had a remaining esotropia on looking straight up and an exotropia on looking straight down. When first observed, these results were disconcerting, since it was felt that an extremely unstable condition had been produced, with the possibility of the straight eyes in the central field changing into an exotropia or back into an esotropia at any time. While these early postoperative cases were being watched with anxiety, other cases of esotropia with bilateral depression in adduction were seen in which glasses alone corrected the deviation. These fully accommodative cases had straight eyes and stereopsis in the primary position but also had an esotropia on looking up and an exotropia on looking down.

TABLE 7.—*Effect of Horizontal Muscle Surgery on Up and Down Position of Gaze*

Operation	No. of Cases	Average Degrees of Reduction of Esotropia		No. of Cases with Reduction of Esotropia		
		Up	Down	Up=Down	Up>Down	Up<Down
Resection one lateral rectus.....	3	13	0	..	3	..
Resection both lateral recti.....	9	12	5	3	5	1
Resection one lateral rectus and recession one medial rectus.....	27	18	24	5	4	18
Resection both lateral recti and recession one medial rectus.....	3	36	18	..	3	..
Resection one lateral rectus and recession both medial recti.....	2	32	27	..	2	..
Recession both medial recti.....	6	24	32	1	1	4

The follow-up of the postsurgical and the accommodative cases, for as long as eight years in some instances, has led us to believe that this condition is a stable one. The eyes have remained straight in primary position, and the esotropia on looking up and the exotropia on looking down have persisted.

The possibility must be considered that the ability of the eyes to adjust themselves for different deviations may be mediated through a special psychooptical reflex, whose function is the maintenance of a balance in the center. This was suggested by the stability of the balance that was maintained not only for opposite deviations in upward and downward gaze but also in looking to the right and to the left in some cases. This reflex for a balance in the center may be related to the midpositioning phenomenon or centering of the eyes in cats and monkeys as described by Bender and others.[2]

Since it has been nearly impossible to straighten the eyes in cases of esotropia with bilateral depression in adduction in all positions of gaze (only 2 out of 65 cases), it may be best to operate in the following manner: Enough resection of the lateral rectus muscles, unilateral or bilateral, is done to obtain a small remaining esotropia on looking up and enough recession of the medial rectus muscles, unilateral or bilateral, to obtain a small exotropia on looking down. This will produce optimum conditions for the postulated reflex of a balance in the center to take effect, and the eyes should become straight in primary position. Two exceptions will be (1) cases that have an exotropia on looking down to begin with and (2) certain cases with straight eyes for near and good fusion but with

an esotropia on looking up and for distance. In these cases only the resection of the lateral rectus muscles should be done as the primary procedure. It was in this latter type of case that it was possible to obtain straight eyes in all positions.

SUMMARY

Following surgery in 65 cases of esotropia with bilateral depression in adduction and greater deviation for distance and upward gaze than for near and downward gaze, the eyes became straight in the primary position in 40 cases, 16 cases had undercorrection, and 9 had overcorrection. In only two cases did the eyes become straight in all positions of gaze. In 25 cases the eyes were straight in primary position but had an esotropia on looking up which balanced an exotropia on looking down. This was seen not only postsurgically but also in many accommodative cases. A psycho-optical reflex has been postulated for this balance in the straight-ahead position of the eyes. To arrive at this balance in cases which require surgery, it is suggested that resection of one or both lateral recti be considered for those cases of relatively little esotropia, mostly present on upward gaze. Larger amounts of esotropia may also require recessions of one or both medial recti, which should be done conservatively if the esotropia on downward gaze is relatively small.

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The Histopathology of Iris Pigment Changes Induced by Miotics

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Formation of nodular excrescences along the pupillary border coincident with pilocarpine and physostigmine therapy was first reported by Vogt in 1920.[1] Except as a medical curiosity, the anomaly received little attention until the advent of more potent miotics. Following introduction of isoflurophate (DFP; di-isopropyl fluorophosphate), Abraham reported a high incidence of these nodules after miotic treatment, particularly in children.* Isoflurophate has been receiving widespread use in the treatment of accommodative esotropia, as well as in the treatment of glaucoma.† Swan has reported cases in which the resulting combination of severe miosis and large pupillary nodules temporarily interfered with vision, but generally the nodules have been considered to be transitory and relatively innocuous.[4] They have been observed to disappear within a few weeks or months after treatment.

Insight into the pathogenesis and nature of the nodules developing during miotic treatment has been largely limited to speculation. From the clinical appearance and similarity to iris cysts experimentally produced in animals,[5] most authors have considered the nodules to be cysts formed by separation of the two layers of iris pigment epithelium at the pupillary margin. Some authors have assumed that these changes were confined to the pupillary border of the iris and that edema induced by intense contraction of the iris sphincter was the precipitating factor. We also considered this to be the most likely explanation until recently, when we obtained new data from two patients. One of these patients, a 16-year-old boy with congenital aniridia and secondary glaucoma, was receiving daily instillation of 0.1% isoflurophate in olive oil. Nineteen months after the beginning of treatment two typical pigmented nodules appeared at the border of the rudimentary iris near the chamber angle and steadily enlarged until miotic treatment was terminated. The iris was immobile, so that miosis could not have been a factor in development of the pigment nodules in this case.

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From the Department of Ophthalmology of the University of Oregon Medical School (Drs. Christensen and Swan).

* References 2 and 3.

† Abraham.[3] Knapp, P.: Personal communication.

Fig. 1.—Gross specimen. Note excrescences on pupillary ruff.

Recently we have had the opportunity to study microscopically the pigment changes which occurred in a human eye after prolonged miotic therapy. The findings in this case bring up new aspects of the problem and merit a detailed report.

REPORT OF A CASE

In 1955 the eye of a 9-year-old boy was submitted to the John E. Weeks Memorial Laboratory at the University of Oregon Medical School. The boy had been treated for unilateral congenital glaucoma since infancy. Shortly after birth he was found to have an enlarged globe and elevated intraocular pressure. Therapy consisted of local instillations of 1% pilocarpine nitrate solution. This was subsequently changed to 2% pilocarpine nitrate and finally to a 1% physostigmine hydrobromide solution. In the ensuing years the child was under the care of several physicians, so that it was not possible to obtain the details of his medication; however, over a nine-year-period miotics were used intermittently whenever a rise in tension was noted. On Aug. 11,

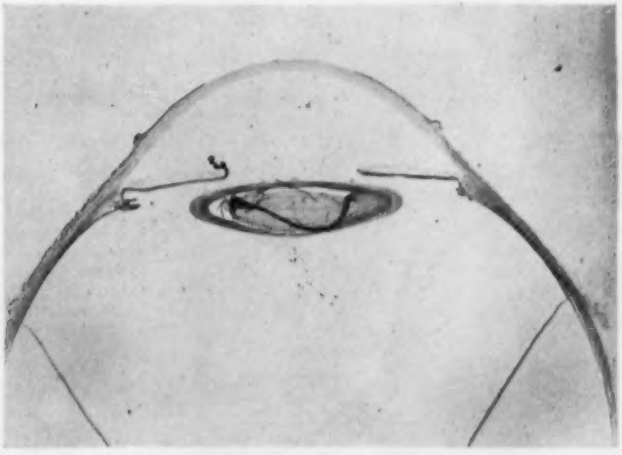

Fig. 2.—Section through membranous proliferation of pigment epithelium of pupil on one side. Reduced to about 60% of mag. × 8.

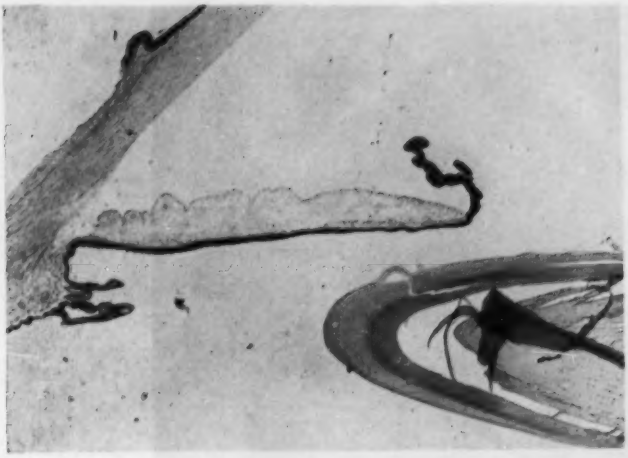

Fig. 3.—Higher-power magnification of Figure 2. Reduced to about 60% of mag. × 26.

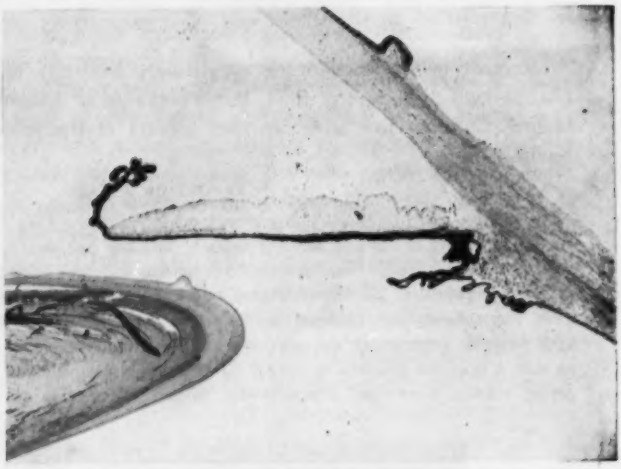

Fig. 4.—Section through terminal cystic nodule. The cystic space was filled with pigment-containing fluid. Reduced to about 60% of mag. × 26.

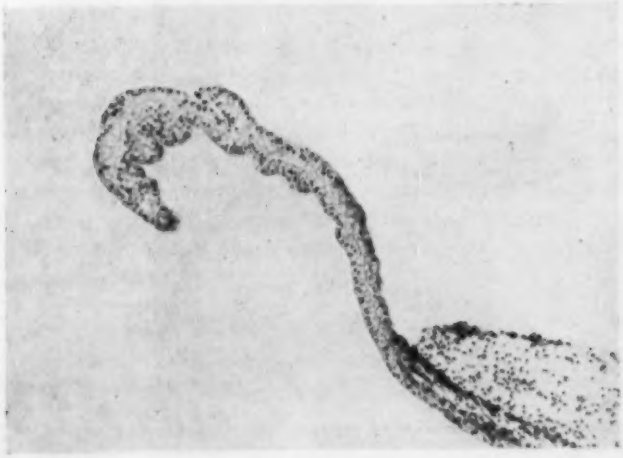

Fig. 5.—Bleached section of membranous proliferation. Note distinct definition of two cellular layers. On the iris the anterior cell layer is flat and indistinct. When free of the iris, this layer becomes as thick and velvety as the posterior layer. Reduced to about 60% of mag. × 80.

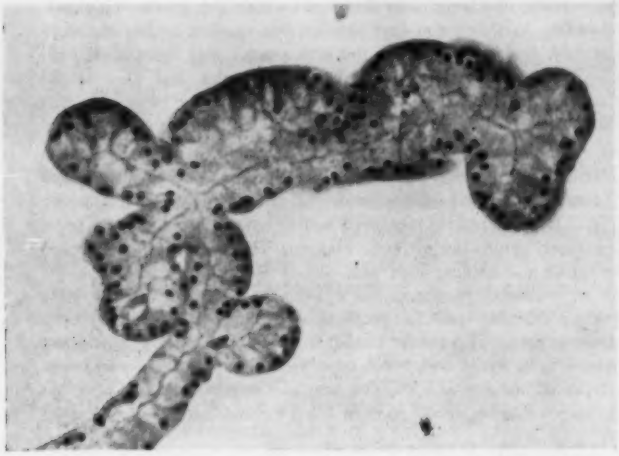

Fig. 6.—Higher-power magnification, demonstrating cell detail. Reduced to about 60% of mag. × 320.

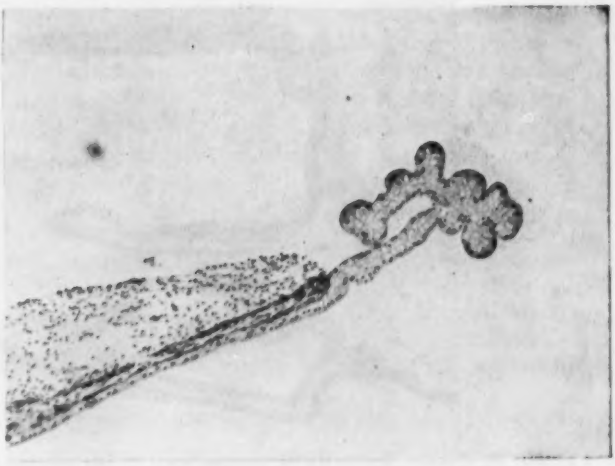

Fig. 7.—Bleached section through branching area of proliferation. Reduced to about 60% of mag. × 80.

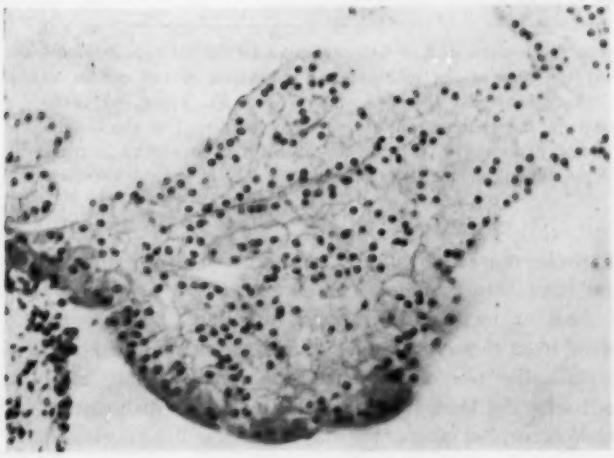

Fig. 8.—Bleached section through terminal nodule. Reduced to about 60% of mag. × 320.

1954, "a small, black, pigmented, tentacle-like body" was observed extending from the iris pupillary border into the anterior chamber. Within three days similar, but smaller, bodies appeared on either side of the original nodule. By January, 1955, the entire pupil was "garnished with small pupillary excrescences." The sudden appearance of these nodules and their rapid development in an enlarged glaucomatous eye led to an enucleation. Malignant melanoma was considered in the differential diagnosis.

Pathological Report.—Gross examination of the specimen revealed a firm, regularly shaped left eye, measuring 26×26×25 mm. The cornea was clear. The anterior chamber was deep and free of cells and debris. Several pigmented masses protruded into the pupil and anterior chamber from the iris ruff (Fig. 1). Each nodule measured approximately 1 mm. at its base. When the globe was opened, a clear, semijelled vitreous escaped. The optic nerve appeared elevated and yellow-white. The retina and lens were in situ.

Microscopic study revealed an enlarged, glaucomatous eye in which there was a viable retina and optic nerve. Finger-like pigmented epithelial projections extended from the pupillary border of the iris into the pupillary area and anterior chamber (Figs. 2, 3, and 4). In some sections these projections appeared as a flat, two-layered membrane, but in others there was branching of the membrane or terminal nodules or both. This was best demonstrated in bleached sections (Figs. 5, 6, 7, and 8). In some areas small pigment-filled cystoid spaces were formed

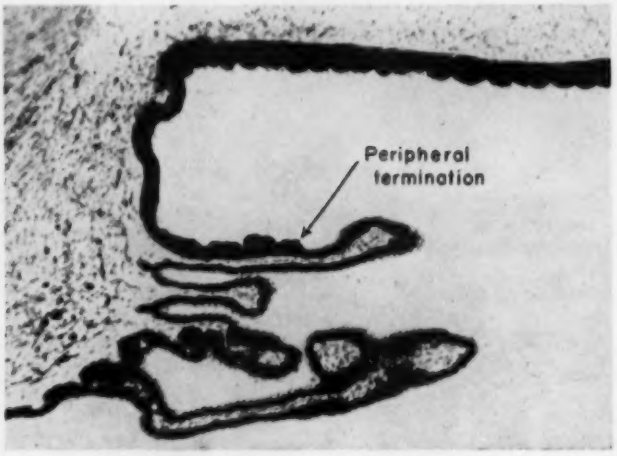

Fig. 9.—Section demonstrating encroachment of iris pigment epithelium on ciliary process. (This may be normal.) Reduced to about 60% of mag. × 96.

by splitting of the epithelial layers. Hyperplasia of iris pigment epithelium did not appear limited to the pupillary area alone. At the root of the iris, pigment epithelium spread out in an apron-like extension onto the ciliary body and ciliary processes (Fig. 8). These extensions also were finger-like and similar to the growths on the pupillary border. The significance of this extension along the ciliary processes is difficult to assess, since a similar pattern, although possibly less extensive, is not uncommon in normal globes. There was no alteration of iris stroma or muscle.

COMMENT

Several features of this specimen are particularly interesting. Until the present time these pupillary nodules have been considered as simple cysts that probably formed from secretion of fluid or mechanical irritation associated with severe miosis; however, it is evident from this globe and our patient with aniridia that extreme miosis cannot explain the phenomena adequately. In addition, most authors have been concerned with the least significant feature of the disturbance, that is, cyst formation. Cysts do occur, but most of the excrescences in this enucleated

eye were solid nodules composed entirely of pigment epithelial cells. Furthermore, the cysts which were formed contained fluid permeated with pigment rather than clear fluid, as previously supposed. Of greater significance than the cysts was the new growth of the iris pigment epithelium beyond the borders of its normal limitations. This growth was highly selective, since there was no obvious effect on other structures of the iris or ciliary body. To our knowledge, extension of the epithelium beyond the limits of its supporting mesoderm into the anterior chamber has no parallel in response of the other ocular tissue to medicinal therapy. This proliferation of pigment epithelium is the most intriguing of the tissue changes observed and stimulates most thought, since it is a hyperplasia that borders on neoplasia. Finally, when treatment is discontinued, these nodules recede. The mechanism of this recession is as much a mystery as their formation, but in all probability they undergo simple atrophy following cessation of stimulation.

SUMMARY

From a microscopic study of an eye which developed pupillary pigment nodules during prolonged miotic therapy, it appears that miotic drugs stimulate a proliferation of the iris pigment epithelium beyond limits of its normal development. This proliferation may form a two-layered membrane, small nodules, or epithelial cysts and may interfere with visual acuity in miosis. The mechanism of this reaction is not known; however, it is not due solely to hypersecretion or mechanical irritation of the pigment epithelium induced by miosis. The nodules were noted in an immobile rudimentary iris of congenital aniridia. The proliferation may be a selective tissue response to parasympathetic stimulation.

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Neurilemoma of the Ciliary Body

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The neurilemoma, a benign nerve sheath tumor, has been reported in the orbit a number of times.[1] Intraocular examples, however, are rare. The following case is reported for this reason, and, in addition, the clinical history is of considerable interest, since the tumor in this instance closely simulated an intraocular malignant melanoma.

REPORT OF A CASE

A 68-year-old white woman, was admitted to Strong Memorial Hospital on Nov. 14, 1949, for a cataract extraction. Her only complaint was impaired visual acuity at distance and near in the right eye. This was first noted about two years previously.

Positive physical findings were limited to the chest, where a faint apical systolic murmur was heard.

The ocular examination showed a corrected visual acuity of 20/200 O. D. and 20/30 —4 O. S. The external structures were normal; the pupils were of equal size and reacted promptly to light. Slit-lamp examination revealed bilateral anterior and posterior subcapsular lens opacities, more advanced on the right. No fundus details were discernible on the right, and the left fundus was normal. The intraocular pressure was within normal limits in each eye, and no evidence of inflammatory activity was noted on slit-lamp examination.

An intracapsular lens extraction, through a round pupil, was accomplished without difficulty. At the time of operation, shortly after the delivery of the lens, a tumor mass was noted in the lower temporal quadrant of the fundus, which appeared to be a cystic or solid neoplasm of the ciliary body.

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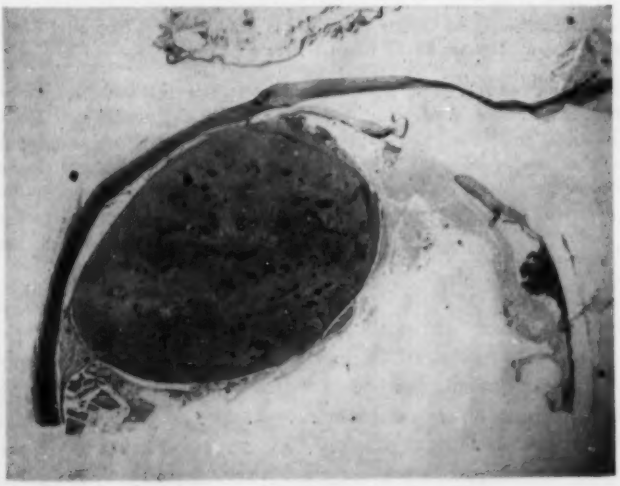
From the Division of Ophthalmology, Department of Surgery, University of Rochester School of Medicine and Dentistry.

Fig. 1.—Neurilemoma of the ciliary body. Reduced to 78.5% of mag. × 6.



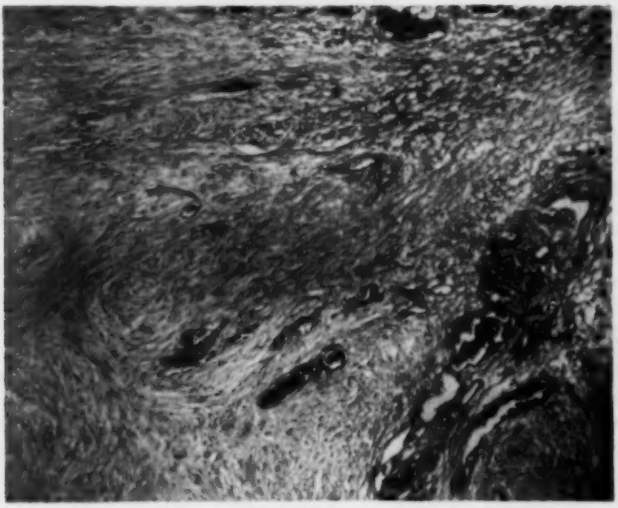


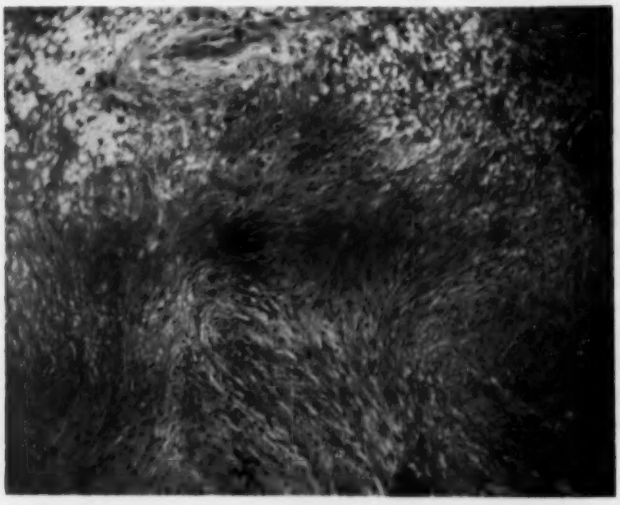
Fig. 2.—Neurilemoma of the ciliary body. Reduced to 78.5% of mag. × 100.

After an uneventful postoperative course, the mass was examined under the slit-lamp, and it appeared rounded, smooth, and dark-brown in color. It extended from 6 to 8:30 o'clock along the maximally dilated pupillary border and reached about one-third the distance between the pupillary border and the visual axis. Transillumination was not impaired. Visual acuity with an aphakic correction was 20/40—2. At this point it was felt that the lesion was a cyst of the ciliary epithelium.

Over the following three years the eye was examined at frequent intervals, and, in view of the normal pressure and normal tranillumination, as well as the absence of inflammatory signs, a diagnosis of benign cyst seemed justified.

By June, 1953, however, several dilated subconjunctival vessels had made their appearance in the quadrant overlying the lesion. Also, the iris now bulged forward slightly at that site.

Fig. 3.—Neurilemoma of the ciliary body. Reduced to 78.5% of mag. × 100.



The intraocular pressure remained normal, and the slit-lamp appearance and gross size of the lesion appeared unchanged.

During the next seven months the vessels became more prominent and the pressure rose to 30 mm. Hg (Schiøtz). At this point a faint aqueous flare and occasional cells were noted in the anterior chamber. With the onset of glaucoma and inflammatory signs, the impression of benign cyst seemed untenable, and the clinical diagnosis was changed to malignant melanoma of the ciliary body. Enucleation of the eye was deemed the proper course, and this was performed on March 4, 1954.

The enucleated globe was of normal size and on section presented a solid, gray-colored tumor of the ciliary body (Fig. 1). The mass was egg-shaped, some 6×10 mm. in size, and extended from the equator to the posterior surface of the iris.

Microscopic sections revealed a thinly encapsulated tumor of the ciliary body over which ciliary muscle and processes, as well as Bruch's membrane, extended without interruption. The tumor cells were grouped into interlacing streams and whorls, with palisading of nuclei a conspicuous feature. The intervening relatively acellular areas presented many microcysts of various sizes, as well as large vascular channels. The nuclei of the individual cells were pale-staining, basophilic, and ovoid in shape for the most part. Phosphotungstic acid-hematoxylin and Masson stains demonstrated sparse amounts of collagen scattered throughout the tumor. No pigment or evidence of mitotic activity was noted. There were a few foci of lymphocytes and plasma cells in the choroid. The microscopic picture was that of a neurilemoma—the cellular areas corresponding to the Type A tissue of Antoni, while the relatively acellular portions with microcysts and large vascular spaces comprised the Type B tissue of Antoni (Figs. 2 and 3).

In retrospect, we do not feel that there were any points which would allow a distinction to be made clinically between this tumor and a malignant melanoma.

COMMENT

The various classifications of nerve sheath tumors have been based on topographical and histological differences between the lesions, as well as malignant potentialities. As a result, a confusing array of terms and synonyms has evolved. Minckler,[2] for instance, gives the following classification for tumors arising from nerve sheaths: (1) neurofibroma; (2) perineural fibroblastoma; (3) neurinoma (Schwannoma or neurilemoma); (4) acoustic neuroma; (5) multiple neurofibromata (von Recklinghausen's disease); (6) neurogenic sarcoma.

In considering the common benign nerve sheath tumors, Stout[3] champions the Schwannian origin of these lesions, and, while objecting to the term neurofibroma (he would prefer diffuse neurilemoma), he would clarify the classification of the benign nerve sheath tumors by considering only the terms neurofibroma and neurilemoma. He believes that there is sufficient difference in the growth characteristics, histological arrangement of the cells, ease of successful removal, and chances of malignant change to warrant keeping the two important forms of benign nerve sheath neoplasms separated.

Further, the names perineural fibroblastoma and Schwannoma reflect the long-standing debate concerning the nature of the parent cell in these benign tumors of nerve sheath origin. Penfield[4] and his school favor the fibroblast as the cell of origin, whereas Stout[3] believes in the Schwannian derivation of the type cell. A mesodermal as opposed to a neuroectodermal origin is thus postulated. From time to time each school has brought forth evidence to support its stand, such as the differential staining studies of Tarlov,[5] in favor of the first theory, and Murray's[6] tissue-culture work, supporting the neuroectodermal theory.

This study has concerned itself with reported examples of solitary intraocular nerve sheath tumors, unassociated with von Recklinghausen's disease. Under discrete neurofibromata, Duke-Elder[7] lists the cases of Axenfeld and Nitsch, the neurinoma reported by Kyrieleis, Callender and Thigpen's case of two neuro-

fibromata in the same eye, and Papoleczy's intra- and retrobulbar tumor of this type. Other examples he cites are those of Freeman, Stough, and Moorehouse. Trevor-Roper [8] reported an intra- and an extrabulbar neurofibroma.

SUMMARY

A case of a solitary benign nerve sheath tumor (neurilemoma) of the ciliary body is reported, and the terminology of nerve sheath tumors is discussed briefly.

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The Stallard Iridencleisis Operation

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When Stallard was in this country several years ago and lectured at the Wills Eye Hospital on what he chose to call "anterior flap sclerotomy with basal iridencleisis," we were particularly impressed with the high percentage of his surgical successes in glaucoma. After seeing his movie, we decided to use this procedure in selected cases. We now report on 48 patients who have undergone operation in one or both eyes for glaucoma.

At first we were at a loss to know just which cases to select for this procedure. Stallard, in his original report,[1] and, more recently, in his more complete report of 1953,[2] used the procedure in all types of primary glaucoma, regardless of whether the angle was wide or narrow. He also operated in some cases of acute congestive glaucoma during the acute attack. We still prefer a basal iridectomy, peripheral or complete, in acute congestive glaucoma. In the majority of patients with chronic glaucoma we have done his operation. We should like to refer to it as a Stallard iridencleisis. We realize that this procedure is not entirely original with him but is, rather, a modification in principle of others previously performed by other ophthalmic surgeons.

In general, the eyes we selected were those one would otherwise consider likely candidates for the Elliot trephination, iridenclesis, Lagrange's or Iliff's sclerectomy, or other types of filtering operations. We shall not discuss the various tests and observations necessary in the diagnosis of glaucoma and the indications for surgical intervention. We include only patients with primary glaucoma for whom we considered that surgery was indicated.

While some of our iridencleises patients have been Negroes, in general we have preferred to do the Elliot trephination in this group. Our exact reasoning here is somewhat obscure. We do know that members of the Negro race throw out more pigment and are more prone to a keloid type of scar formation following surgery than are the lighter-pigmented races. While we cannot prove it, it is our impression that a larger, round opening is less likely to become obstructed in the Negro than is a wound with inclusion of a piece of iris. In general, our indications for the Stallard iridencleisis operation at this time is chronic glaucoma in patients of the white race.

SURGICAL TECHNIQUE

The operation can be performed quite satisfactorily with local anesthesia. An O'Brien block is used, with tetracaine or, more recently, Ophthaine (2-diethylaminoethyl-3-amino-4-propoxybenzoate), by instillation. A retrobulbar block is not used, as it is not necessary to control pain, and such a procedure has the added disadvantage of lowering the intraocular pressure. It has

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been our experience that a high-normal or slightly elevated tension makes iris inclusion surgery less difficult than if the eye has normal tension or is hypotonic at the time of surgery; consequently, a miotic is not usually given on the day of operation, although a miotic pupil is desirable at the time of surgery.

After routine preoperative operation of the lids, the eye is draped, a speculum is inserted, and an antiseptic flush is used. A suture is then placed under the superior rectus muscle. A small amount of procaine is then injected beneath this muscle. Care is taken not to penetrate the superior rectus with either the suture or the injecting needle, as a hemorrhage in this muscle can be an annoying complication of the surgical procedure.

An incision 8 to 10 mm. long is made through conjunctiva and Tenon's capsule down to bare sclera. This incision is located at the insertion of the superior rectus tendon. A flap is then dissected down to the limbus. All bleeding is then controlled with pressure and/or epinephrine. A cautery is used only if absolutely necessary. A scratch incision is then made 3 mm. from the limbus and parallel with it. When this scratch is approximately one-half to two-thirds of the way through the sclera, a traction suture—000000 nonabsorbable (silk) surgical suture—is placed through the anterior scleral lip of the incision. Again, any hemorrhage is controlled, as it is our belief that most blood in a chamber following this type of surgery seeps in from the outside; the prevention of its entering the chamber is easier than its evacuation once it has gained access to the chamber. The scratch-down incision is then continued until the base of the iris is seen. The direction of incision should be at right angles to the surface of the globe at the line of incision (Fig. 1). This means that, since the eye is rotated downward, the handle end of the cutting instrument (we use a Bard-Parker knife with a #15 blade) needs to be angled from the vertical toward the feet of the patient.

Fig. 1.—Incision through conjunctiva and Tenon's capsule with scratch incision in sclera.

A narrow cyclodialysis spatula is used to check the extent of the incision depth. Ideally, when the grayish-black root of the iris or the beginning of the ciliary body comes into view, the spatula is used to dialyze the ciliary body from the scleral spur. Care must be taken that the base of the iris is not penetrated, with the resulting embarrassment of the spatula being behind the iris. This complication is not always easy to avoid in cases of long-standing narrow-angle glaucoma with a dense synechia. It can usually be avoided by closely hugging the inner scleral and corneal surfaces as the spatula enters the eye. A cyclodialysis is then performed by repeated poking thrusts, as advocated by O'Brien,[3] rather than by attempting to sweep the angle; this latter method is usually attended by a greater danger of hemorrhage.

Once the cyclodialysis is completed as far as can be reached in either direction from the incision (this usually being one-third or less of the circumference of the globe), the scleral incision is hinged. This hinging is done with Castroviejo blunt corneal scissors. The scissors enter the incision at one end, with their points directed toward the center of the cornea. One or two snips are made at right angles to the sclera. The hinge is then completed by a similar scissors incision at the other end of the original scratch incision. The width of the hinge is then 2 to 3 mm.; that is to say, the hinge extends to the limbus. We end with a scratch incision that is hinged at the limbus, the width of the base of the hinge being narrower than the original incision (Fig. 2). This convergence of the lateral cuts toward the base of the scleral flap is important in maintaining mobility of the flap on its hinge. The flap is important in maintaining mobility of the flap on its hinge. The flap fails to move on its hinge if the cuts are parallel. It is our impression that the secret of success is in the scleral hinge, which, when held open by the iris, produces a better fistulous tract.

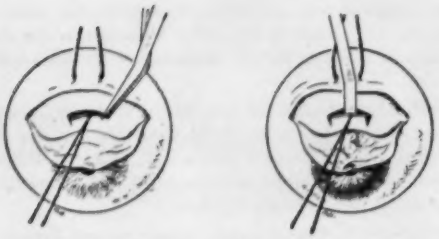

Fig. 2.—The scleral incision is hinged and cyclodialysis performed.

If any blood has entered the chamber, it is gently irrigated out at this time. A toothless iris forceps is then introduced into the chamber, aided by traction on the previously placed suture in the anterior scleral lip. We heartily agree with Chandler that no forceps with teeth should be used in an eye with a clear lens. When the iris forceps is seen to be about halfway to the pupillary margin, the iris is grasped and withdrawn until the sphincter is seen at the surface of the incision. Straight iris scissors are used to cut the iris between the forceps and the sphincter of the pupil. This incision is approximately 2 to 3 mm. in length. A second incision in the iris is then made directly toward the base of the iris at one end of the already incised iris. A third similar incision is then made at the other end of the original iris incision (Fig. 3). In effect, we now have a dialyzed ciliary body without dialysis of the base of the iris from the ciliary body, the iris

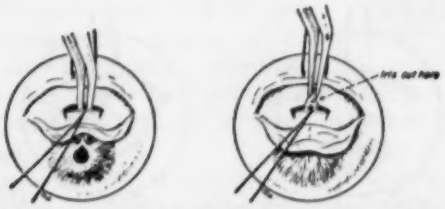

Fig. 3.—Iris grasped and basal iridectomy done.

sphincter remaining intact. The peripheral half of the iris for a width of 2 to 3 mm. has a flap which is hinged at its base. This iris flap is then left incarcerated in the wound with the pigmented undersurface of the iris now facing upward. Gentle irrigation or light corneal massage with an iris spatula is used until the pupil becomes round, indicating no lines of tension on the included piece of iris.

The original incision is closed with a running black 000000 nonabsorbable (silk) surgical suture, care being taken to include Tenon's capsule, as well as conjunctiva, in the closure (Fig. 4).

No drops are placed in the eye at the completion of the operation. Only the eye operated on is patched. A wet cotton splint is used and a shield is applied.

Fig. 4.—Iris is included in wound and overlying incision is closed.

The chamber is usually formed at the first dressing 24 hours later, at which time the pupil is dilated with 4% homatropine hydrobromide. Hydrocortisone drops are used daily at rounds. The patient is up and around two days following surgery and is discharged on the fourth or fifth postoperative day, usually on hydrocortisone drops only. No massage is used.

RESULTS

The advantages of this type of iridencleisis, according to Stallard,[2] are as follows:

1. The anterior chamber is re-formed in 24 hours.
2. There is no need for postoperative massage.
3. In seven days a bleb is formed which has a thicker covering than is the case with a trephine opening.
4. The operation successfully reduced the intraocular tension within 25 mm. Hg in 97.7% of his series of 162 eyes.

AGE GROUP OF 62 EYES IN 48 PATIENTS

40 - 50	10	20.8%
51 - 60	18	37.5%
61 - 70	11	22.9%
71 - 80	9	18.5%

Fig. 5.—Age group of patients operated on.

SEX

MALE	FEMALE
26	22

RACE

WHITE	BLACK
41	7

Fig. 6.—Sex and race incidence.

Lukic [4] further states that the iridencleisis technique, with maintenance of the normal form of the pupil, has both functional and esthetic advantages over the technique employing section of the sphincter.

Our own results were as follows:

We performed the operation on a total of 62 eyes, in 48 patients. The age group incidence was about what one would expect with glaucoma patients: There were 20.8% in the 40- to 50-year group, 37.5% in the 51- to 60-year group, 22.9% in the 61- to 70-year group, and 18.5% in patients more than 71 years of age (Fig. 5).

Twenty-six patients were men and 22 were women. Forty-one patients, or 70%, were white, and seven patients, or 30%, were Negroes (Fig. 6).

Fifty-eight, or 93.5%, of the 62 eyes operated on had their glaucoma controlled postoperatively. Thirty-one of the 58 eyes (53.4%) were controlled by surgery alone.

Twenty-seven, or 46.6%, of the 58 eyes whose tension was normalized, however, required miotics in order to maintain normal tension, without loss of vision or reduction of the visual field. Of the four failures, three eyes had secondary glaucoma (Fig. 7).

We realize that our total number of eyes operated on is small and that the follow-up period is relatively brief. The average follow-up time is 22.4 months.

CONTROL OF GLAUCOMA

58 of 62 EYES CONTROLLED POSTOPERATIVELY 93.5%

31 of 58 EYES CONTROLLED BY SURGERY ALONE 53.4%

27 of 58 EYES CONTROLLED POSTOPERATIVELY BUT

REQUIRED MIOTICS 46.6%

(3 of 4 FAILURES WERE SECONDARY GLAUCOMAS)

Fig. 7.—Results of surgical control of glaucoma.

No attempt is made to compare results of the Stallard iridencleisis operation with those for any other type of glaucoma surgery. It is our aim to do this in a later communication. In this preliminary report we have attempted to evaluate the efficiency of the Stallard iridencleisis operation.

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Bilateral Indentation of Cornea and Lens

A Unique Developmental Anomaly

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Developmental abnormalities of curvature of cornea or lens are usually regular and possess symmetry; that is, the curvature is either increased or decreased with a regularity that permits of measurement, or at least description in geometric terms. In microcornea, cornea plana, and microphakia, the radius of curvature of the entire surface is either increased or decreased to a visible extent beyond the normal range. In keratoconus and anterior and posterior lentiglobus, only a circumscribed portion of the surface shows the deviation, but the deviation itself, with the exception of some rare cases of peripheral posterior lentiglobus,[1] is sufficiently regular to be described fairly accurately as either conical or hemispherical in shape. On the other hand, instances of circumscribed abnormalities of curvature possessing no geometric regularity are rare. The following case presents several such irregularities of the surface curvature and is recorded because of its uniqueness and the problems it poses as to etiology.

REPORT OF A CASE

The patient, a 61-year-old white man, had no complaints relative to his eyes when seen on routine examination for pension purposes. During service in World War I his vision, according to Army records, was 20/20 in both eyes, and he first began to wear glasses shortly after the war. Neither since that time nor before had he had occasion to visit an ophthalmologist except for change of glasses.

Gross inspection of the eyes revealed an indentation of the anterior surface of each cornea in its lower third, extending across more than half the breadth of the cornea in this region (Fig. 1*A*). The backward bowing of the indentation extended deep enough for the lower lid to fit snugly, on downward gaze, into the recess formed, so that the normally curved portion of the cornea appeared to rest on the full thickness of the lower lid margin, the skin surface of the lower lid and the anterior surface of the normally curved cornea being almost in the same curved plane (Fig. 1*B*).

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Fig. 1.—*A*, A. P. view of both corneas, showing location and extent of indentations. *B*, lateral view, showing relation of lower lid to cornea on downward gaze.

The details revealed by slit-lamp examination are shown in Figure 2*A*. The backward bowing of the anterior corneal surface is seen to be rather sharp, creating a definite roof for the indentation. The indentation itself ocupies approximately two-thirds of the breadth of the cornea, displaced somewhat nasally, and merges gradually into the limbus inferiorly. The anterior corneal surface is still concave as it joins the sclera.

The posterior surface of the cornea does not present any pronounced abnormality of curvature similar to that of the anterior surface. In the upper portion of the cornea the relation between the two surfaces appears quite normal. However, at a point just below the level of the "roof" of the indentation, the posterior surface begins to diverge from the anterior surface more rapidly than it would if its curvature were constant. At the limbus the divergence between the two surfaces is strikingly greater than that seen in a normal cornea. The impression gained is that the lower portion of the posterior surface of the cornea has been swung backward as though on a hinge, the rotation taking place about a horizontal axis in the frontal plane, whose cross section is the point, mentioned above, where the two surfaces begin to diverge rapidly.

Another striking feature revealed by the optical section is the unusual thinness of the entire cornea. Superimposed on this thinness is the "waist" across the cornea, created by the backward bowing of the anterior surface toward the still normally curved posterior surface at this level. As a result, the cornea at the "waist" is so thin that the separation of a thin vertical line of midstromal opacity from the anterior and posterior surfaces by a minute thickness of clear stroma on each side can just about be perceived. There is also an opacity of the posterior surface in the region of the "waist." The cornea is otherwise clear.

On gonioscopy, the angle was open, and no unusual tissues or structures were seen. The anterior chamber appeared deep, and the iris presented no abnormality of structure or position.

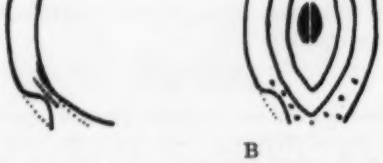

Fig. 2.—Schematic optical sections of cornea and lens. Dotted lines indicate normal curvature. *A*, cornea, showing indentation and opacities of posterior surface and stroma. *B*, lens, showing indentation, cortical opacities, and intact lines of disjunction.

The impression of backward rotation of the posterior surface of the cornea is strengthened by an interesting finding on gonioscopy of the lower angle. The various structures normally seen on the back surface of the cornea appeared broader than usual; particularly, the band representing the trabeculae appeared quite broad. This is consistent with an increase in obtuseness of the iridocorneal angle that would be produced by backward rotation of the cornea in this region—the more obtuse the angle, the less the foreshortening in the gonioscopic view.

Each lens shows the same backward bowing of its anterior surface as the cornea, although the indentation is somewhat shallower (Fig. 2*B*). It is also not as wide as in the cornea, occupying about half the width of the lens, and is displaced slightly nasally in each lens. The upper border is at approximately the same level as that of the corneal indentation. As in the cornea, the depression continues inferiorly as far as the lens can be seen. There is no return to the original surface level. The abnormal curvature extends backward only as far as the middle of the cortex. Beyond that the lines of disjunction bounding the various nuclei are undisturbed in position and curvature. There are a few small opacities in the anterior and posterior cortex in the region of the indentation. The lens is otherwise clear. In addition to the indentation described, the curvature of the anterior surface of the lens is noteworthy in that the vertical meridian flattens out quite markedly toward the left border of the lens, so much so that the anterior surface appears almost as a straight vertical line in sections in this region. Focusing the cornea and the lens alternately in quick succession, one is impressed with the degree of congruence of curvature of the two indentations. It seems as though the corneal indentation could be superimposed almost perfectly on that of the lens.

The remainder of the examination revealed the following findings:

Visual acuity: O.D.: 10/400, corrected to 20/30 with −6.50D. sph.⌒+11.00 cyl.×180. O.S.: 20/400, corrected to 20/70 with −7.50D. sph.⌒+11.00 cyl.×180. Ocular tension was 20.1 mm. Hg O.D. and 23.4 mm. Hg O.S. (Schiøtz) and exophthalmometric measurements (Hertel) were 17 mm. bilaterally. Each cornea measured 11×11 cm. in its vertical and horizontal diameters. The vitreous was clear, and the fundi were not remarkable. Particular search was made for evidence of developmental defects, but none was found.

Unfortunately, no members of the patient's family were available for examination. Two children—a son, 30 years of age, and a daughter, aged 32—reportedly have no eye trouble and do not wear glasses.

COMMENT

There have been very few cases reported of irregular abnormalities of curvature of either cornea or lens.

Mann [2] mentions three cases of umbilication of the lens. Her description is as follows:

This [umbilication of the lens] is a rare condition. It has been seen in a dogfish embryo and I have only been able to find two cases in man. . . . In all three cases, the abnormality involved the posterior surface of the lens. This showed a small shallow depression not necessarily central, nor associated with an opacity. The most likely explanation seems to be that certain of the lens fibers do not attain their full length and fail to meet each other at a suture, which thus forms a shallow gutter or depression instead of being a smooth join. This was borne out by Burdon Cooper's case, in which a shallow trough-like depression was present in a position corresponding to one of the lower limbs of the posterior Y. The reason for the aberration is unknown and it is too rare to postulate anything further.

Fig. 3.—Umbilication of the lens. Redrawn from Figure 232, in "Developmental Abnormalities of the Eye," by I. Mann, published by the Cambridge University Press, London, 1938.

Figure 3 is a copy of the sketches accompanying the above description.

Another form of irregular abnormality of curvature was originally reported by Koeppe.[3] He described closely packed, crater-like depressions of the posterior surface of the cornea, separated from each other by thin, sharp-edged ridges, occurring in patches and extending almost to the limbus. He compared them with the appearance of the moon's surface as seen through a telescope. No further mention is made of this anomaly in the literature.

It has been assumed that the unusual deformities in the present case represent a developmental anomaly rather than an acquired defect because of their symmetrical bilaterality, the absence of any disease entity that could possibly yield such an end-result, and the fact that a plausible explanation on an embryological basis can be offered. The only entity that could be considered here in differential diagnosis is marginal degeneration of the cornea,[4] also known as ectatic marginal dystrophy or peripheral furrow keratitis. This produces a corneal deformity strikingly similar to the one seen in this case. However, it can be eliminated from consideration on several grounds. The present case does not have the characteristic opacities of the anterior surface; there is no vascularization of the cornea here; the deformity in this case extends straight across the cornea instead of following the curve of the limbus, and, most important, this entity does not affect the lens.

In seeking to formulate a theory as to the mode of development of this unusual deformity, the chief problem consists in explaining how two structures which are

distant from each other (anterior surfaces of the cornea and the lens) can suffer congruent deformities and yet an intervening structure (posterior surface of cornea) not be deformed in the same way, even possess a curvature in the opposite direction. The solution appears given if one postulates that the two surfaces are in close enough apposition to each other, at some time, to suffer deformities simultaneously by the application of a single force and that, at a later date, a third structure is interposed between the original two. These conditions, with the exception of the deforming force, are given in the normal development of the embryo. Between the 3.2 and the 10 mm. stage, the lens vesicle develops and separates from the surface ectoderm. The surface ectoderm gives rise to the corneal epithelium. Later, at the 18 mm. stage, the paraxial mesoderm from the region of the margin of the optic cup insinuates itself, in three waves, between the surface ectoderm and the lens and gives rise to the corneal endothelium, corneal stroma, and iris stroma. One need assume only the presence of a deforming force or influence at the stage when the lens vesicle is separating, or has just separated, from the surface ectoderm. Both structures will then suffer more or less congruent deformities, the lens perhaps to a less marked degree and extent, since it is further removed from the deforming force. When the paraxial mesoderm later begins to extend into the space between lens and surface ectoderm, it finds this space already encroached upon by the backward bowing of the surface ectoderm. In changing the course of its advance slightly by veering posteriorly to avoid this obstruction, it produces the hinged effect of the lower part of the posterior corneal surface described above. It should be noted that the location of the corneal indentation in each eye corresponds approximately to the region of the surface ectoderm from which the lens vesicle is pinched off.

No opinion is offered as to the nature of the deforming force. Whether it was an external pressure applied bilaterally or an inherent defect in the cells of the surface ectoderm is too speculative a question to be answered on the basis of a single case and without opportunity for histological study.

The unusually high degree of astigmatism is considered to be due to the same deforming force as that which has been assumed to have given rise to the more obvious deformity.

SUMMARY

1. A case presenting symmetrically bilateral and almost congruent indentations of cornea and lens is reported.

2. The meager reports in the literature, indicating the rarity of any type of irregular abnormality of curvature of cornea or lens on a developmental basis, are briefly summarized.

3. A theory is proposed to explain the mode of development of the described indentations.

Dr. Jacques Landesberg, Chief of E.E.N.T. Unit of the Brooklyn V. A. Regional Office, discussed this case with me.

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Teflon Implant to Elevate the Eye in Depressed Fracture of the Orbit

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AND
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The use of various implant materials for correcting subluxation of the globe and restoring maxillary contour in fractures of the orbital floor has been under constant consideration by ophthalmic surgeons. Impetus for such investigation has been provided particularly by World War II, when many defects of this type presented themselves in casualties from high-explosive shells, land-mine explosions, and other causes. A survey of the possible means of correcting such defects discloses a variety of implant materials and techniques, many of which have offered indifferent results, and others hold promise of providing a satisfactory solution to the problem. From the abundance of implant agents which have been employed, a few might be mentioned.

Fresh costal cartilage is recommended by Spaeth [1] to be placed, when possible, beneath the periosteum in order to lift the eye. Pierce * uses cartilage from the cadaver. Fat implants, it is generally agreed, undergo a certain amount of absorption, although they may increase in size, according to Weidler.[2] Bone from the ileum is sometimes used.

Inanimate objects are more easily obtainable that body tissue. Devoe [3] used glass wool packed under the periosteum. Ruedemann [4] has used tantalum mesh. Suker [5] injected paraffin into Tenon's capsule as a late implant after enucleation, but this substance sometimes changed its position or was occasionally extruded. Sherman [6] used acrylic wedges to raise the eye out of the depressed fracture of the orbital floor. He inserted them beneath the periosteum. Souders [7] used flat, rhomboid-shaped plates of acrylic placed above the periosteum, rather than beneath it, and held in position by sutures.

LeVeen and Barberio [8] tested FM-1 nylon, Celluloid, Lucite, and Teflon by implanting finely divided particles of these substances into the peritoneal cavity of dogs. When a large surface was presented to the tissues by this finely divided state, substances previously thought to be nearly innocuous were found to arouse a considerable inflammatory reaction. A layer of protein was found to be adsorbed on the surface of all the plastics except Teflon. LeVeen and Barberio point out that if protein or water is adsorbed on the surface of a plastic or metal, the molecular configuration must necessarily be altered from that of the adjacent tissues. They believe this to be the cause of the foreign body reaction. They also

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Teflon is obtainable from the Polymer Corporation of Pennsylvania, Reading, Pa.
From the Department of Ophthalmology, the Reading Hospital.
* Pierce, cited by Spaeth,[1] p. 94.

believe too little attention has been paid to the effect on tissues of physical characteristics of implants, as in the case of metals, in which the galvanic effect can cause tissue necrosis. They quote the works of Gortner and Briggs,[9] who showed that glass in contact with water carries a high electronegative charge on its surface, but that if the glass is coated with paraffin, which cannot be wet by water, the charge is zero.

Of the plastics tested by LeVeen and Barberio, Teflon alone did not adsorb a protein film nor can it be wetted with water. It alone produced no foreign body reaction in the abdominal cavity of animals. When Teflon was implanted, there was a striking absence of all round cells, giant cells, and fibrous tissue around its particles. After six weeks the particles of Teflon were found lying loose and free in the folds of the omentum instead of being fixed to it, as was the case with FM-1 nylon, Celluloid, and Lucite.

Of thousands of plastics, only a few are used in medicine. To avoid confusion, even among these few, the following list may be helpful.

1. Methylmethacrylate, chemical name polymethylmethacrylate, also called acrylic resin. It is sold under the trade name of Lucite by Du Pont, of Plexiglas by Rohm and Haas, and of Perspex by the British.

2. Nylon (Du Pont), chemical name polyamide of hexamethyleneamide and adipic acid.

3. Polyethylene (chemical name) is sold under the trade name of Alathon by Du Pont and of Bakelite by Union Carbide and Carbon Corporation.

4. Polytetrafluoroethylene (chemical name) is sold under the trade name of Teflon by Du Pont and of Fluon by the British.

Because it is innocuous to tissues and has other desirable characteristics as an implant agent, Teflon was chosen as the substance to implant into an orbit to elevate a ptotic eye and to insert on the anterior maxillary surface to build up the depression of this region in a case which it is the purpose of this paper to report.

CHARACTERISTICS OF TEFLON

Teflon is polytetrafluoroethylene resin. It is white; the surface feels waxy, and it can be whittled and shaped with a sharp knife like soft wood. It is the most chemically inert plastic ever developed; it has no known solvent, is unaffected by boiling in nitrohydrochloric acid (aqua regia), and is equally resistant to strong alkalis. It is stable at temperatures up to 620 F (327 C) and can therefore be autoclaved. When heated above 620 F, Teflon gives off poisonous fumes; so it should not be incinerated. Teflon has relatively high tensile strength, is flexible, has a "memory," and undergoes nearly complete recovery from a deforming load. Nothing will stick to Teflon with any appreciable strength, and water will not wet it.

REPORT OF A CASE

The patient, a 50-year-old farmer, while attempting to give medication to a steer, was attacked by the animal, which struck him on the left side of his face with its head. Subsequently the man's left eyelids swelled shut, and he noted great tenderness and swelling over the left maxillary region and inferior orbital rim. During the next few weeks the swelling and tenderness subsided, but he then had a disfiguring depression of the left eye to a level below that of the right eye and double vision, which prevented him from working (Fig. 1).

He reported for treatment three months after his injury occurred. The left eye was 4 mm. lower than the right. No extraocular muscle paresis could be detected. The left maxilla was pushed downward and backward, causing depression of the medial two-thirds of the lower orbital

Fig. 1.—Eight months after accident. Floor of left orbit displaced downward and backward, with ptosis of left eye.

rim. The x-ray report was as follows: "The examination of the facial bones shows evidence of a depressed fracture involving the left maxillary bone, with the inferior border of the orbit depressed posteriorly and with slight separation of the suture line between the orbital processes of the frontal and zygomatic bones. There is also depression of the anterior portion of the zygomatic arch. Diagnosis: fracture of the left maxilla."

Since three months had elapsed after the injury, the fractured maxilla had become fixed in its displaced position and could not be restored by traction.

It was necessary to correct the diplopia by raising the left eye with an implant beneath the globe into the orbit, and it was desirable to fill out the depression of the left maxilla with a similar implant on the anterior maxillary surface beside the nose.

Fig. 2.—Implants cut from the large piece of Teflon, which is 8 mm. thick, 38 mm. wide, and 100 mm. long. The cut pieces measure on an average 25 mm. across and 30 mm. vertically. The holes are 3 mm. in diameter. Edges are wedge-shaped. The two interlocking pieces next the Teflon bar were implanted, the arrow-shaped part, above, going into the orbit, the lower part being used to fill out the cheek.

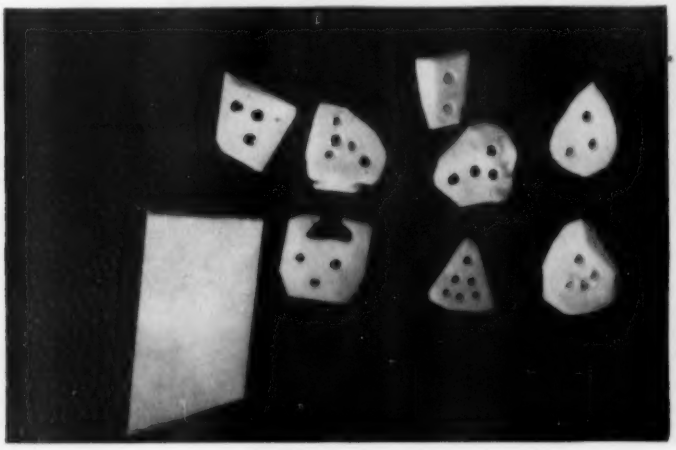


Fig. 3.—Arrow-shaped implant, which was inserted horizontally into the orbit.

Prior to operation, which was performed eight months after the injury, a number of implants were prepared in the following manner: A piece of Teflon 8 mm. thick was sawed into triangular pieces (Fig. 2) 20 mm. wide at the base and 18 mm. from base to apex. These were then shaped with a knife to fit the bony defect in the floor of the orbit. The implants were shaped so as to fit closely against the medial orbital wall, on one side, and to avoid encroaching on the inferior orbital fissure, on the other (Fig. 3). The actual size of the bony defect was estimated by noting the proportion of the orbital floor which appeared depressed in the x-ray picture and transferring these proportions to a skull skeleton to obtain relatively exact measurements of the size and shape of the plastic implant necessary to fill in the depression. Very little subsequent shaping was necessary at operation.

Since nothing will adhere to Teflon, a number of holes 3 mm. in diameter were bored in the implants to permit ingrowth of tissue for anchorage.

Operation.—With the patient under thiopental (Pentothal) sodium anesthesia, a horizontal incision through skin and muscle to the bone was made 8 mm. below and parallel with the inferior orbital margin of the left eye. The orbital septum was then incised horizontally in its center for 3 cm. and the orbital contents lifted with a periosteal elevator for a depth of about 3 cm. For implantation into the orbit a triangular piece of Teflon, as described previously,

Fig. 4.—The vertical implant for the maxillary surface interlocking with the horizontal implant.

Fig. 5.—Vertical implant extending downward anterior to the maxilla. It is joined at a right angle with the horizontal implant, which fills the depressed orbital floor.

was selected, on the end of which a keystone-like projection had been fashioned with a knife. This projection interlocked with a similarly cut receptacle in the upper end of a piece of Teflon destined to extend vertically down from the orbital margin over the anterior surface of the maxilla (Fig. 4).

The first piece of Teflon was inserted into the orbit beneath the eye, where, because the orbit is a closed space except in front, it not only lifted the eyeball but brought it forward. Next, the dissection was carried down over the surface of the maxilla external to the periosteum, and a second piece of Teflon, which interlocked with the first, was inserted vertically to fill out the depression of this region (Fig. 5). Through several holes made with a nail drill in the implants at the orbital margin, the former were attached to the periosteum with a white cotton suture on a curved needle.

The muscles and fascia were closed with interrupted 0000 chromic absorbable surgical suture. The skin edges were united with a subcuticular nonabsorbable (silk) surgical suture.

A pressure dressing was applied for three days. When this was removed, little swelling was noted but a great deal of ecchymosis was present. At first the left eye was nearly fixed

Fig. 6.—Reaction fourth day after operation.

in the orbit and could not be rotated in any direction (Fig. 6). Motion returned during the following four weeks, however, and diplopia disappeared. The postoperative reaction of the tissues was only that which would be expected from the surgical trauma.

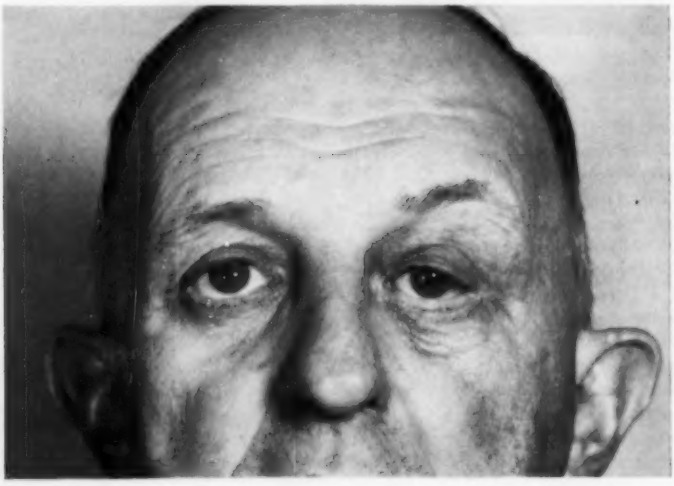
Four months after operation there was no inflammatory reaction from the Teflon implants discernible by inspection. The patient has had no discomfort (Fig. 7).

SUMMARY

A case report is presented in which Teflon, a tetrafluoroethylene resin, was used as an orbital implant to correct ptosis of the eye following orbital fracture, with these advantages:

1. It does not cause any inflammatory reaction in the surrounding tissues.
2. It is unaffected by temperatures of 620 F and can therefore be autoclaved.

Fig. 7.—Two months after operation. The vertical implant can be felt deep in the tissues. No tenderness, inflammation, or edema was present.



3. It has no known solvent and is chemically the most inert plastic known.

4. Its consistency is such that it can easily be cut and shaped with a knife at operation.

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Clinical Notes, New Instruments and Techniques

SIMPLE LAST STEP OF EXENTERATIO ORBITAE

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CONWAY * described two cases in which the defect was covered by a graft of skin. In the third case "the surgery was carried out by an exenteration and radical excision, but the defect was closed in a different way. The soft tissues were elevated from the forehead and relaxed by the use of horizontal incisions, which were carried through the periosteum and the fibers of the frontalis muscle, but not through the skin. Similarly, the soft tissues were separated from the anterior aspect of the maxilla, using the periosteal elevator. Mobilization of the soft tissues of the upper and lower portions of the wound was effected by this technique, so that the defect could be closed by linear suture, in horizontal direction. The relaxation of the upper flap by the use of the hidden relaxation incisions is the effective step in this technique. This method recognizes the fact that dead space, provided by the cavity of the orbit, must eventually fill with serum and blood. The effect of such a concentration of fluid is fibrosis, which results in a dimpled surface. The remnant of the eyebrow is dislocated downward."

To the method of closing an orbit after exenteration I may add a few words: First, in the 16th edition (1939) of the "Lehrbuch der Augenheilkunde" by Ernst Fuchs,[2] I advised as the finishing step of an exenteration of the orbit the following procedure: "Then the conjunctiva or, if the entire conjunctiva and the lids had been removed, the skin is exactly sutured and a slight pressure dressing is applied. The orbit is filled thus with blood, which later becomes organized and retracts the skin somewhat. In this way the cavity of the wound can be covered in a short time (two weeks)." †

With this simple method the exenteration of the orbit does not involve a prolonged, and usually very painful, after-treatment.

In connection with Conway's third case, I may mention that for closure of a very large defect, in which both lids have been entirely removed, a simpler procedure is possible. In 1928 I operated on a woman, 38 years of age, who had black disseminations of melanosarcoma (malignant melanoma) in the right upper and lower fornices of the conjunctiva; the tumor had started to develop on the inner angle of the lids five years before. Both lids, the skin of the right side of the bridge of the nose, the tear sac, and the ductus lacrimalis and orbital tissue were removed. Then I undermined with a knife the skin of the forehead and of the cheek, without touching the periosteum or the frontal muscle, until with my hand I was able to push the cheek so far upward that the skin corresponding to the lower orbital margin touched what was left of the upper lid. While my assistant kept the cheek in this position, I united the upper and lower lips of the wound in a linear suture. I was not able, however, to cover the defect of the inner angle, where an area less than the size of a nickel remained uncovered. After application of boric acid-petrolatum (Vaseline) and a piece of gutta-percha to the operating field, all the time the cheek being pressed upward by my assistant, I pulled the cheek to the forehead by several strips of strong adhesive plaster; I did not exert then special pressure, as such pressure was already exerted by the plaster strips. Seven days later I loosened the upper ends of the plaster strips while the assistant pressed

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* Conway, H.,[1] read before the New York Academy of Medicine, Section of Ophthalmology, Nov. 15, 1954.

† The same sentences can be found on page 872 of the 17th edition (1944) and of the 18th edition (1946).

the cheek upward without a moment's relaxation. I looked at the suture and removed the stitches. Without further procedure, I fixed the same ends of the plaster on the forehead again. The same pressing of the cheek upward was done when I examined the wound on the 11th day. I did the same thing on the 14th day. At this time the wound was healed; only at the inner angle, between the bridge of the nose and the former lids was there a spot, 4 mm. in diameter, filled with granulations. I applied another dressing to pull the cheek upward and sent the patient back to Rumania, where she had come from. When I saw the woman five years later, the orbit was closed by soft skin, showing a slight indentation. No scar was visible on it; the eyebrow was not pulled down.

The fact that in the case reported by Conway the eyebrow was dislocated downward, whereas in my case the eyebrow remained on its original, normal, place, is probably due to the incisions through the frontalis muscle.

One can see from this case of mine that special incisions through periosteum and frontalis muscle are not essential.

Plantastrasse 19.

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A NEW TYPE OF OCULAR PROSTHESIS

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THE PURPOSE of this paper is to report the experience in fitting 50 blind, unsightly eyes with a cosmetic contact shell.[1] Four specific cases are reported in detail by way of illustration. Failures in the past have been due to the technical limitations of fabricating a contact shell thin enough to avoid producing an apparent exophthalmos in the eye covered by the cosmetic shell, especially where an ocular deviation is present. Thus, the fitting of this type of prosthesis has been limited to enophthalmic eyes. During the past few years a new processing technique has been developed whereby an ordinary plastic contact lens is converted into a cosmetic shell, with a thickness of 0.5 mm. or less. In this way, a variety of unsightly eyes have been fitted which in the past had defied prostheses.

Fitting of this type of prosthesis should not be construed as a substitute for enucleation. It is indicated only where there is no danger to the patient in the retention of the sightless eye and in those cases in which enucleation is refused.

METHOD

All the patients in this series were referred to my colleagues and me by ophthalmologists. An ordinary contact lens was first fitted over the eye for a trial period of one to two weeks to determine the patient's toleration of the lens and his ability to care for it properly. No patient was fitted with a cosmetic shell who did not tolerate the contact lens during the trial period, or who could not take proper care when inserting or removing the lens. If, after the two-week trial period, no adverse reactions were encountered, the anterior surface of the contact lens was transformed by a series of mechanical and art procedures into a cosmetic contact shell that conformed in appearance with the healthy eye. The patients were followed at bimonthly intervals to determine their tolerance of the prosthesis.

The construction and fitting of this type of prosthesis differ from the previous procedure in the following way:

1. A prosthesis of acrylic plastic is fitted with the posterior surface contacting the scleral portion of the globe, and allowing for very slight corneal clearance.

2. The periphery is sufficiently deficient to prevent slippage in extreme excursions of the eye.

3. The prosthesis has an anterior-posterior thickness of from 0.3 to 0.5 mm. at the corneal and limbic region, to permit normal palpebral fissure formation.

4. The anterior surface of the prosthesis is reconstructed after proper fitting of the posterior surface. If any convergence or divergence of the eye is present, a new corneal position is created centrally.

METHOD OF CONSTRUCTION

So that ophthalmologists may aid the contact lens and ocular prosthesis technician in fabricating a cosmetic contact shell, the following basic steps are given:

1. A scleral-type contact lens is fitted to the blind eye. This may be done from a trial contact-lens-fitting set, except where irregularities of the sclera exists, in which case an impression of the eye should be taken by an experienced contact lens technician, and a scleral

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Figure 1

Figure 2

Figure 3

lens fitted first to a positive copy of the eye involved. The patient should wear the lens intermittently for approximately one week to determine his tolerance, and also his ability to insert and remove the lens. All adjustments should be made before fabricating the cosmetic lens.

2. A negative copy is made of the trial contact lens, and an exact positive of the lens is molded in acrylic plastic, pigmented to match the sclera.

3. With the sclera-colored lens placed in position on the patient's eye, the exact location of the pupil is marked with wax pencil onto the anterior surface of the lens. The diameter of the iris is measured and the average pupillary width decided upon.

4. The proper iris size is scribed onto the anterior surface of the scleral lens, using a sharp-pointed compass. The pupillary aperture is enlarged to conform to the size decided upon. This is done with a dental drill or rat-tail file.

5. The color and striae of the natural iris are painted within the scribed margins, and the blood vessels and modifying colors of the sclera are reproduced, as is done in regular artificial-eye fabricating. The artificial iris, scleral color, and veins are fixed onto the lens by baking at 100 C in an oven.

6. After approximately six hours of baking, the lens is placed on the original mold and a quick-curing dental acrylic, pigmented with lampblack, is pressed into the aperture made to accommodate the pupil. When the black plastic used to simulate the pupil has hardened, a thin layer of clear acrylic plastic is processed over the anterior surface of the shell. After the prescribed curing time for acrylic plastic has been observed, the lens is removed from the mold and polished.

REPORT OF CASES

Case 1.—A woman aged 18 was referred with a diagnosis of calcereous degeneration of the right cornea, with 25 degrees of exotropia. The right eye had been blind since the age of 5 years and had gradually become divergent. A cosmetic contact shell was successfully fitted over the right eye (Fig. 1*A* and *B*) in August, 1955. She tolerates the prosthesis well and is able to wear it for one week without removal. The epiphora, present before, disappeared after fitting of the contact shell. *C* and *D* (Fig. 1) illustrate the excellent motility obtained.

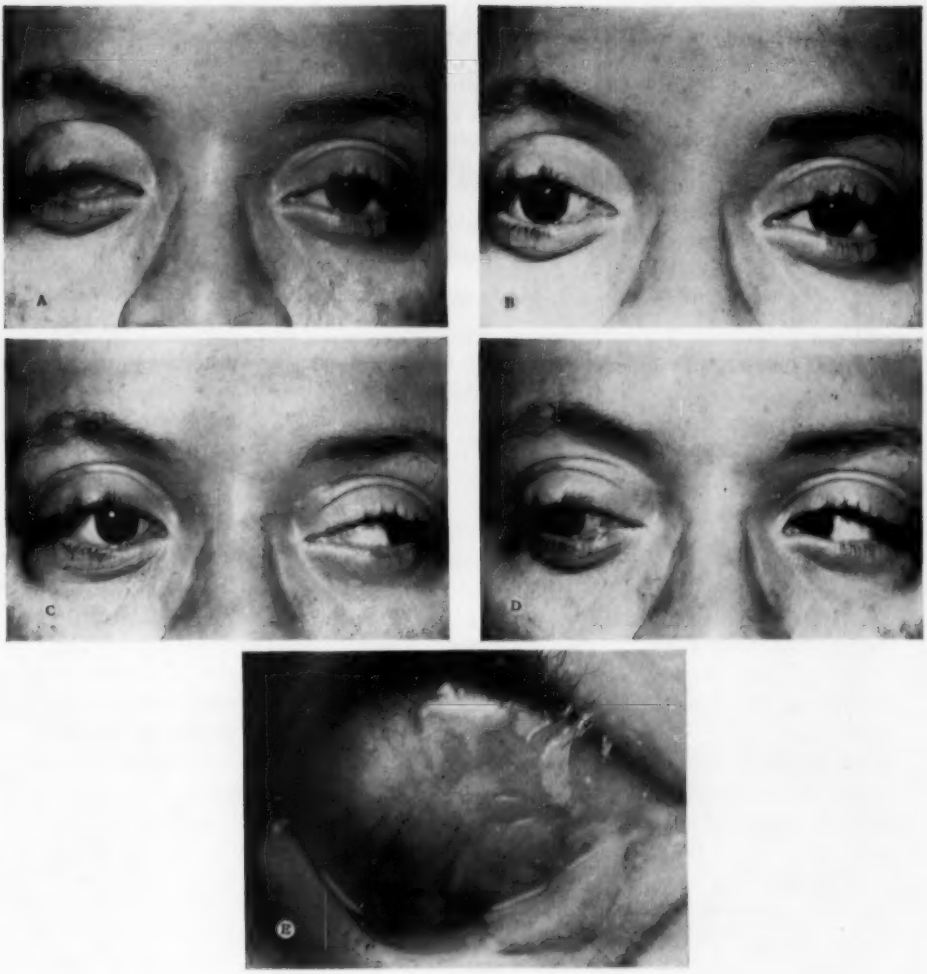

Figure 4

CASE 2.—A girl aged 11 years was referred with a diagnosis of a blind right eye and blood-filled cornea. The patient was successfully fitted with a cosmetic shell (Fig. 2*A* and *B*) in December, 1955, and has worn the prosthesis symptom-free to the present time. Her wearing time is all day, with removal at bedtime. *C* and *D*, Figure 2, illustrate the motility of the prosthesis.

CASE 3.—A woman aged 40 was referred with the diagnosis of calcareous degeneration of the cornea, left eye, following injury. Attempts had been made to fit the patient with a regular shell prosthesis, without success. In June, 1955, a contact cosmetic shell was fitted (Fig. 3*A* and *B*), with a good cosmetic result, and the patient's wearing time is two weeks. *C* and *D* of Figure 3 illustrate the motility.

CASE 4.—A patient, aged 25, was referred with a diagnosis of lye burn of the right eye. The eye was blind and shrunken, with extensive symblepharon formation (Fig. 4*A* and *E*) involving both lids. An initial attempt was made to fit the patient with a regular shell prosthesis, without success, because of the discomfort caused by the periphery of the prosthesis being

fitted to the limited cul-de-sac. In July, 1955, a contact cosmetic shell was fitted without discomfort (Fig. 4*B*, *C*, and *D*). The patient wears the prosthesis for periods up to eight weeks without removal.

SUMMARY

Four cases are reported from a series of 50 in which a new type of prosthesis has been successfully fitted over blind, unsightly eyes. The method of construction and fitting is described, and patients on whom unsuccessful attempts at prosthesis fitting had been made previously have worn this new type of prosthesis comfortably, with excellent cosmetic results.

55 E. Washington St. (2).

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Annual Reviews

DISEASES OF THE RETINA AND OPTIC NERVE

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THE LITERATURE on diseases of the retina and of the optic nerve during 1955 followed much the same pattern as in previous years. The actual number of articles on subjects with bearing on these portions of the ocular structures is so tremendous that it would be impossible to cover them all in a review of reasonable length. An individual reviewer can do little more than include a cross section of papers which were of interest to him. Admittedly, this review does not represent a complete bibliography, particularly of the very voluminous foreign literature.

RETROLENTAL FIBROPLASIA

In spite of the fact that little really new was added to our knowledge of retrolental fibroplasia during the past year, the number of articles published continued to increase. Most of the papers deal with the question of oxygen administration, and there is still no unanimity of opinion on the subject. The clinical course of the disease is generally agreed to follow the pattern outlined by Owens,[1] the first, or vascular, stage being characterized by dilatation and tortuosity of the retinal vessels, with areas of neovascularization peripherally. However, Patz [2] states that in infants receiving oxygen in 60% to 70% concentration there is an initial stage of marked attenuation or obliteration of the retinal vessels preceding the stage of vasodilatation. Owens [1] notes that the active phase of the disease usually subsides by the age of 6 months and that spontaneous regression occurs in seven-twelfths of cases before proliferation of vessels into the vitreous begins. Tabor, Shaul, and Graves [3] state that the progress of retrolental fibroplasia may be arrested at any stage of development but that regression has not been observed to occur after neovascularization is advanced or the retina is detached.

Pathology.—Friedenwald [4] outlines the histologic changes that are recognized to be characteristic of retrolental fibroplasia. Infants with incomplete retinal vascularization are susceptible to the disease. The first recognizable histologic lesions are regions of avascularity associated with regions of patchy overgrowth of the retinal capillary endothelium, with the formation of glomerular tufts of varicose capillaries and patchy proliferation of spindle-shaped mesenchymal cells. In later stages, hemorrhages and transudation appear around these abnormal vessels, and the vascular proliferation bursts out of the retina into the vitreous. Retinal detachment results in part from the transudative process and in part from fibrosis of the vascular strands in the vitreous. There is little specifically characteristic in the cicatricial stage; fibrotic remnants of the so-called glomerular tufts may still be recognizable and may help in establishing the diagnosis.

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Relation to Oxygen Therapy.—Kinsey and Hemphill [5] analyzed the results obtained in studies conducted in 18 hospitals located in different parts of the United States. The incidence of retrolental fibroplasia in infants who received oxygen in concentration of at least 50% for 28 days was compared with that in infants to whom oxygen was given only on the basis of frank clinical need. All other conditions of care were the same in the two groups. Active stages occurred in 72% of the routine-oxygen group and in only 30% of the curtailed-oxygen group. The cicatricial stage developed in 25% of the routine group and in only 6% of the curtailed-oxygen group. Kinsey and Hemphill think that these findings are sufficiently definite to establish that the incidence of retrolental fibroplasia is positively associated with the use of oxygen and that the deleterious effect of oxygen is noted particularly when oxygen is used during the first 10 days of life. Limiting the amount of oxygen to that required for clinical emergencies did not affect the survival rate of the premature infants. Engle and Levine [6] agree with the latter finding, viz., that oxygen need not be administered routinely to small premature infants. They state that they have not detected any late ill-effects from the early termination of oxygen administration.

Further data indicating the positive association of retrolental fibroplasia with oxygen therapy are supplied in papers from various parts of the world (Blix,[7] Brændstrup,[8] Brændstrup and Flensborg,[9] Brehme,[10] Fenwick,[11] and Rosner [12]). Several authors agree that the administration of oxygen plays a part in the etiology of retrolental fibroplasia but think that some other factor or factors may be at least partly responsible. Among these authors are Aalde and Imerslund,[13] Gómez Vila,[14] Huggert,* and Zanén, Meunier, and Piraux.[15]

Silverman [16] notes that the majority of observers agree that the incidence of retrolental fibroplasia is related to the degree of prematurity. He calls attention to some of the characteristics of premature infants, such as anemia, marginal anoxia associated with irregular or periodic breathing, instability of the body temperature, impairment of fat absorption and of renal function, and electrolyte imbalance. He points out that fetal hemoglobin differs qualitatively from adult hemoglobin in its unusual ability to take up oxygen at low oxygen pressures. A longer time is required to convert fetal hemoglobin to adult hemoglobin in the premature than in the full-term infant. The incidence of hemangiomas is higher in the more immature infants, but no connection has been established between hemangiomas and retrolental fibroplasia other than the suggestion that the incidence of hemangiomas seems to have decreased since the administration of high oxygen concentrations as a routine measure has been discontinued.

Manschot [17] notes that all anatomic knowledge of the development and proliferation of retinal capillaries favors the view that the first stage of retrolental fibroplasia is due to retinal hypoxia. The proliferation of capillaries takes place in the direction of the vitreous because of the lower oxygen tension there. The respiratory function of the lungs of the premature infant operates under very difficult conditions, and it is hard for the premature infant to develop abnormally high arterial blood oxygen levels even in an environment of high oxygen concentration. Manschot found histologic evidences of an early phase of retrolental fibroplasia in the eyes of three premature infants who had been hypoxic during life, owing to subchronic interstitial pneumonia, corresponding to an advanced stage of the interstitial plasma-cell pneumonia of premature infants. In Manschot's opinion, this pneumonia, which

* Huggert, A., in discussion on article by Blix,[7] pp. 736-738.

occurs apparently epidemically in some clinics in more than 50% of all premature infants, may be the etiologic factor in a considerable number of cases of retrolental fibroplasia.

As a result of their studies of 94 premature infants, Engle and her co-workers [18] conclude that curtailment of the duration of oxygen therapy and reduction of the concentration of oxygen are not accompanied by a reduced incidence of active or cicatricial retrolental fibroplasia. In their opinion, the duration of oxygen therapy does not determine the susceptibility to the development of the disease. It may influence the severity of the process once it has started, but this has not been proved definitely. The authors state:

> A search in this study for factors other than oxygen which have been implicated in retrolental disease points to the importance of low birth weight, immaturity (especially those born at a gestational age of 29-30 weeks) and "anoxia" or poor condition at birth as important determinants.

They regard the maturity of the infant at birth, and therefore the stage of fundal development, as the crucial pathogenetic factor, and they suggest that obstetricians be encouraged to make every effort to prolong pregnancy beyond the crucial period of 29 to 30 weeks of gestation.

Oxygen Weaning.—Opinions vary on the value of oxygen weaning in the prevention of retrolental fibroplasia. Reese [19] states that there is not sufficient evidence to prove that the rate of withdrawal from oxygen affects the ultimate outcome. In the opinion of Kinsey and Hemphill,[5] prolonging the infant's stay in oxygen for gradual weaning increases the risk of development of retrolental fibroplasia. On the other hand, Tabor, Shaul, and Graves [3]; Aalde and Imerslund,[13] and Zanén, Meunier, and Piraux [15] favor gradual discontinuance of the oxygen. Bedrossian, Carmichael, and Ritter [20] state that none of 30 infants with some stage of retrolental fibroplasia showed any evidence of the disease while receiving oxygen. They regard improper withdrawal of oxygen as a significant, and the commonest, precipitating factor in the development of retrolental fibroplasia. They note that a group of premature infants who were removed suddenly from an atmosphere of 50% oxygen had a significantly higher incidence of retrolental fibroplasia than did another group of premature infants who had gradual diminution in the concentration of their oxygen environment.

Oxygen in Treatment of Retrolental Fibroplasia.—Blodi [21] states that there is no effective medical treatment of the disease and advises only treatment of such complications as may arise, particularly secondary glaucoma. Reese [19] states that evidence is lacking that retrolental fibroplasia is benefited by oxygen therapy. However, Aalde and Imerslund [13] and Manschot [22] report successful results from oxygen therapy. Manschot states that oxygen should be readministered if retrolental fibroplasia appears after withdrawal of oxygen. A concentration of 40% probably will suffice to reestablish a normal retina. This concentration should be reduced very gradually and increased again if changes appear. Bedrossian, Carmichael, and Ritter [20] regard the retinopathy of prematurity as a primarily anoxic disease; oxygen administration predisposes to the disease through its constricting effect on the growing retinal vessels. They think that, after the disease has started, oxygen therapy is of value in most cases if judiciously used and withdrawn gradually. Seven infants were given oxygen therapy because their retinopathy was becoming progressively worse; all improved rapidly and definitely.

Late Results of Retrolental Fibroplasia.—Truhlsen [23] reports that retrolental fibroplasia was the cause of the blindness in 20 of 41 blind children of preschool

age in Nebraska. He states further that in 26 states it has been found that this disease was the cause of 50% or more of the cases of blindness among preschool children. Krause [24] reports the findings in a follow-up study of 107 children who had had retrolental fibroplasia. Their ages at the time of the follow-up ranged from 4 to 17 years. Thirty-six (34%) were retarded mentally to some extent. Seventeen (16%) were in a state institution for retarded children. About 70% had vision of 5/200 or less. About 60% had myopia of more than 5 D., and about 40%, myopia of more than 10 D. Nine of the children had died; necropsy did not reveal any characteristic histologic brain lesions.

Fletcher and Brandon [25] state that 21 of 22 babies with high myopia whom they observed had had retrolental fibroplasia. They note that premature infants with retrolental fibroplasia have high myopia early in the course of the disease. The myopia decreases gradually but increases secondarily between the third and the sixth month to between 10 and 20 D. In their group of cases, this degree of myopia has been sustained for two or more years. They suggest that an underlying metabolic disturbance in the media produces changes in the axial length, corneal curvature, and index of refraction, which account for the myopia of prematurity. Planten [26] reports a case of retrolental fibroplasia in which the terminal picture was that of a falciform fold of the retina.

Silverman [16] states: "Systemic manifestations of retrolental fibroplasia have not been uniformly reported and associated changes in other organs are denied by most students of this disease." He notes also that there is no evidence of an increased incidence of mental retardation in children with retrolental fibroplasia. Parmelee [27] studied the developmental pattern of 28 infants who were blind as a result of retrolental fibroplasia. Two of them were grossly retarded. In the others, it was noted that sitting without support, standing alone, and walking alone were definitely delayed, seemingly because of dependence on vision for balance. Smiling, putting objects in the mouth, pulling to a stand, and walking while holding on followed the established norms more closely.

Scott [28] reports that in a series of 240 premature babies weighing 4 lb. (1814 gm.) or less 23 developed retinopathy of prematurity and 10 true spastic diplegia; 5 had both retrolental fibroplasia and spastic diplegia. He regards the retinopathy of prematurity as part of a general cerebral disorder resulting primarily from anoxemia. Ingram and Kerr [29] report that among 1257 surviving premature infants there were 21 with retrolental fibroplasia, 6 of whom had cerebral diplegia, and 29 with cerebral diplegia, 6 of whom had retrolental fibroplasia. The severity of the diplegia, the extent of the retrolental fibroplasia, and the degree of impairment of mentality were roughly parallel in the six cases. Ingram and Kerr state that, while both retrolental fibroplasia and cerebral diplegia are likely to occur in premature infants, it appears probable that the frequency of the association of the two conditions in this group was greater than could be accounted for by chance. They suggest that anoxia in the prenatal, natal, and postnatal periods might be important in determining the associated development of retrolental fibroplasia and cerebral diplegia.

Experimental Studies.—In summarizing his experimental studies, Patz [2] states that the fundamental factor in the animal experiments is that the eye is susceptible to oxygen only when the retina is incompletely vascularized and is resistant when vascularization is complete. The effects of oxygen on the incompletely vascularized retina can be divided into an initial vasoconstrictive and obliterative phase and a

secondary proliferative phase. The vasoconstrictive phase is not prevented by cervical sympathectomy preceding exposure to oxygen, by carbon dioxide, or by nicotinic acid. Concentrations of oxygen lower than 40% do not cause vasoconstriction. A lowered oxygen environment corresponding to simple anoxia, even at levels at which many premature infants would not survive, is inadequate to produce the lesions of retrolental fibroplasia experimentally. An anoxic environment causes a slightly abnormal pattern of retinal vascularization, a capillary network denser than normal, and a narrowing of the capillary-free zone about the arterioles, but not vasoproliferation into the vitreous.

Ashton [30] thinks that the vaso-obliterative phase occurs in oxygen, in concentrations over 35%, and that the vasoproliferative phase occurs in air. Both Patz and Ashton agree that detachment of the retina rarely occurs in experimental animals, and Ashton states that, after about five months, the retina becomes completely revascularized, the intravitreal vessels disappear, vision is little affected, and the only abnormalities discernible are an anomalous number and distribution of vessels around the disc. Returning the animals to oxygen during the vasoproliferative phase appeared to control the proliferation; but on subsequent return to air the vasoproliferative process was exacerbated.

Gyllensten and Hellström [31] agree with Ashton that the vasoproliferative changes occur after the return of the animal to air. They found that the tendency to vascular proliferation and to hemorrhage into the retina and vitreous was less the older the animal was when exposure to oxygen was begun. In the avascular retina of the newborn, the proliferative changes were concentrated around the disc. In the older animals the more anterior segments were involved as the vessels grew toward the periphery of the retina.

Apparently, Michaelson and his co-workers [32] were not able to obtain typical neovascularization in mice exposed to high concentrations of oxygen. They found that the extent of vessel outgrowth from the disc was not grossly affected and that the most prominent change appeared to be a delay in formation of the capillary bed around the disc. They think that this may be the early stage of the pathology of retrolental fibroplasia and may explain those cases in which milky pallor of the fundus and optic atrophy are more outstanding than neovascularization.

Brehme [33] expresses the view that the constriction and obliteration of the retinal vessels induced by oxygen are a response to the necessity of maintaining the anaerobic glycolysis that is essential to the retina. Colenbrander [34] thinks that continuous administration of oxygen interferes with the normal rhythmic opening and closing of the capillaries and thus induces anoxemia of the retina. Gyllensten and Hellström [35] studied the effects of general hypoxia on the eyes of newborn mice. They state that their findings do not support the hypothesis that vascular hyperplasia is caused by general hypoxia but also do not justify the conclusion that hypoxia plays no part in the pathogenesis of retrolental fibroplasia.

Cook and Ashton [36] found that the vaso-obliterative effect of oxygen on immature retinal vessels is not influenced in its immediate or its delayed phase by cervical sympathectomy and that the delayed phase is not modified by adrenergic blockade with Dibenamine. Ashton and Cook [37] found that detachment of the retina in the developing kitten leads to an outward proliferation of vessels with the formation of a plexus on the outer surface of the retina, and also to an inward proliferation of vessels with the formation of glomerular tufts in the vitreous. They ascribe these proliferations to a fall in the oxygen tension of the retina resulting from separation

of the retina from the choroid. These investigators [38] found also that detachment of the retina prevents the vaso-obliterative action of oxygen even if a normally effective ambient concentration is maintained for as long as four days. If the animal survives in air after detachment of the retina and exposure to oxygen, the vasoproliferative changes which occur cannot be distinguished from those noted in detached retinas without exposure to oxygen.

Persistent Hyperplastic Primary Vitreous.—Reese [39] describes the clinical and histologic features of persistent hyperplastic primary vitreous and discusses its differentiation from retrolental fibroplasia, retinal dysplasia, retinoblastoma, and congenital cataract. The course of these cases seems to be invariably unfavorable because of the occurrence of spontaneous hemorrhage or the development of swelling of the lens secondary to spontaneous rupture of the posterior capsule. Nothing can be done to prevent or treat spontaneous deep hemorrhage. But eliminating the lens by one or more needling operations can prevent serious and irreversible complications, and making an opening in the fibrovascular sheath permits functioning of the retina, which characteristically in these cases is in place and contains all of its nuclear and fibrous elements and a well-formed fovea.

RETINOPATHY IN DIABETES MELLITUS

Mark and Kaeding [40] compare the retinal findings in rather large groups of normal persons, diabetics, and nondiabetic hypertensive patients. They found that in all groups the incidence of eyeground changes increased with increasing age and that the incidence of senile changes was increased about equally by the presence of diabetes and hypertension. Jensen and Lundbaek [41] describe a pigmentary disturbance at the macula in young persons which resembles senile degeneration and heredodegeneration, but which they think is a true long-term diabetic phenomenon. It was found in 15 of 77 patients below the age of 55 years who had had diabetes for 15 to 25 years. It occurred alone in three patients, in association with microaneurysms and hemorrhages in seven, and in association with microaneurysms, hemorrhages, and exudates in five. It did not interfere with vision.

Fischer [42] compares the systemic findings and the duration of the diabetes in two rather large groups of diabetics, those with and those without retinopathy. He divides the retinopathies into those with hemorrhages only, those with hemorrhages and exudates, and those with retinitis proliferans. He concludes that exudative and proliferative retinopathies are pure diabetic lesions based on predisposition and heredity, and that intercapillary glomerulosclerosis is their counterpart. Hemorrhagic retinitis belongs to the so-called diabetic-promoted lesions and is not especially the early stage of the other types of retinopathy. Also, Fischer [43] studied 42 diabetics with retinitis proliferans. He states that the proliferative retinopathy developed after the age of 50 years in two-thirds of the cases, and that more than two-thirds had had diabetes for more than 11 years. Hypertension was present in 81% and nephropathy in 62%. The vision in most cases was so severely reduced that practical blindness was present. Seven patients were totally blind in one eye and two in both eyes. In 30 of the 42 cases control of the diabetes had been very poor, and in the others it had been questionably poor.

Quiroz and Sauter [44] call attention to the fact that diabetic retinopathy is a specific clinical and histologic entity which is related to the duration, and not to the severity, of the metabolic disturbance. They point out also that the recently demonstrated close correlation between the development of severe retinal lesions

and renal involvement with reduction of renal function and secondary hypertension gives to the retinopathy a more serious general systemic prognostic significance than has been attributed to it previously.

Incidence.—Givner [45] reports that none of 286 juvenile diabetics showed any ophthalmoscopic evidence of retinal vascular disease but that 9 of them (1.5%) had hemorrhages or pinpoint aneurysmal dilatations in the retina. It is the general impression that the incidence of retinal lesions increases with the duration of the diabetes. This impression is confirmed by the reports of Dekking [46] and of O'Donoghue and Drury.[47] Dekking found retinopathy in 26.6% of 383 diabetics. The incidence of retinopathy varied from 1%, in cases of less than 5 years' duration, to 67%, in cases of more than 20 years' duration. O'Donoghue and Drury found retinopathy in 19 of 83 patients who had had diabetes for more than five years. They state that the incidence of retinopathy ranged from 7%, in diabetes of 1 to 5 years' duration, to 60%, in diabetes of more than 20 years' duration. On the other hand, whereas Lisiecka-Adamska and Miratynska-Rusinowa [48] found capillary microaneurysms in 195 of 667 diabetics, they state that there was no relation between the severity or the duration of the diabetes and the frequency of microaneurysms. Microaneurysms were more frequent in nontreated or irregularly treated patients and in younger patients. High blood pressure was not a contributory factor.

Pathogenesis.—Berkman [49] states that the pathogenesis of the capillary lesions in diabetes is unknown and that the significance of elevated serum polysaccharides as one factor in influencing the morphologic features of these lesions remains to be determined. Törnblom and Nordström [50] found that the amount of albumin-bound galactose-mannose in the serum was significantly higher in diabetics with vessel changes in all age groups, but that the albumin-bound hexosamine was elevated only in diabetics less than 50 years of age. Rosen and his co-workers [51] found that there was no significant difference in the xanthurenic-acid output of diabetic patients who have and those who have not developed retinopathy. They found that many diabetics with and without retinopathy were marginally deficient in pyridoxine (vitamin B_6) but that there was no statistical difference between the ones with and those without retinopathy. They tried to induce pyridoxine deficiency in diabetics with retinopathy in the hope of lowering the level of activity of the adrenal cortex. But this was without effect on either the adrenal cortical function or the retinopathy.

Stärck [52] suggests that capillary damage in diabetics is due to an antigen-antibody reaction that results from the occurrence of specific intermediary products of the diabetic metabolism. This is independent of the severity of the diabetes or of the insulin requirements. The adrenals play an important part in this reaction. This concept would explain the development of capillary lesions in mild, or even latent, diabetes. Stärck thinks that changes in serum proteins are another result of the metabolic disturbance and are not the cause of the capillary damage. Allen † says that, histologically, the retinal lesions are seen to be arteriolar or capillary aneurysms of sclerotic weakened vessels not associated with the type of hyaline spheres that are found in the renal glomeruli. He stated:

I strongly suggest that the retinal lesion is not equivalent to the lesion of the diabetic glomerulus, but rather that it is equivalent to the lesion in the afferent renal arterioles, probably containing much lipid, unlike the fully developed lesions of diabetic glomerulosclerosis.

† Allen, A. C., in discussion on article by Berkman,[49] pp. 270-271.

Diabetes in Experimental Animals.—Alagna [53] states that in alloxan diabetes cortisone aggravates and desoxycorticosterone alleviates the symptoms, including the lenticular opacities. While similarities exist between the diabetogenic cataract of experimental animals and that of man, this is not true of retinopathy. Keeney and Barlow [54] note that small hemorrhages and a few discrete exudates were found in the retinas of diabetic animals but that true capillary microaneurysms and retinitis proliferans were not demonstrated. They state, further, that no significant difference could be found in the incidence or severity of retinal changes in alloxan-diabetic rats between those used as controls and those receiving estrone or testosterone. Histologically normal eyes were recovered in similar percentages from all groups of diabetic rats. Neither estrone nor testosterone given in moderately large doses over periods of 2 to 11 months to alloxan-diabetic rats significantly affected the histology of the retina.

Relation of Retinopathy to Control of Diabetes.—Mulholland [55] states that, unfortunately, control has little to offer in the arrest of the retinal or the renal lesions. Tolstoi ‡ followed 44 diabetics for 10 to 13 years on the so-called free diet. No blood sugars were determined. The urine always showed Grade 2 to Grade 4 sugar. Twelve of the patients developed retinopathy (28%, a figure which Tolstoi thinks compares favorably with the incidence of retinopathy in diabetics treated by the rigid chemical technique). Tolstoi states, "These data and nothing else cast doubts on the concept that a normal blood sugar will postpone vascular lesions." However, Kinsell [56] expresses the opinion that a "free diet" is unphysiologic and predisposes to vascular complications. Assuming a diet adequate in other respects, the maintenance of a blood sugar within a physiologic range will significantly decrease the incidence and severity of vascular disease in the diabetic. Evidence is lacking that a high vegetable-fat diet in a nonobese patient in itself predisposes to vascular disease. According to Marble,[57] "This experience with diabetic nephropathy lends further support to the growing conviction that the sequelae of long-term diabetes are related to the degree of control maintained over the years."

Fischer [58] states that the principal factor responsible for the development of diabetic retinopathy is long-standing hyperglycemia and that the best method available at present for prevention of the degenerative complications of diabetes is exact control of the diabetes through training of the diabetics themselves. Dunlop [59] maintained 39 diabetics on a "free diet" for nine years; degenerative complications, including retinopathy, developed in 14 (36%). In a group of diabetics of 15 to 31 years' duration, he found retinopathy in 44% of those with good control and in 79% of those with poor control. He has decided that careful control and aggressive treatment of the diabetes over the years are most important factors in the prevention or postponement of diabetic degenerative lesions.

Treatment of Retinopathy of Diabetes.—An effective medical treatment for diabetic retinopathy has not been found as yet. Keeney and Mody [60] could not demonstrate that carbazochrome (Adrenosem) had any significant effect. Hopen and Campagna [61] failed to obtain a good response from intramuscular injections of trypsin. Gurling [62] did not observe any significant improvement in the retinopathy during treatment with methylandrostenediol, with or without the addition of ganglion-blocking drugs in cases complicated by hypertension. After a trial of Lipoliquid, containing choline, inositol, and cyanocobalamin U. S. P. (vitamin B_{12}),

‡ Tolstoi, E., in discussion on article by Mulholland,[55] pp. 307-309.

in 50 cases of diabetic retinopathy, 15 of them of the proliferative type, Folk [63] concludes that the substance seemed to be of very limited value. Berlin [64] notes that it has been shown that intravenously administered heparin will clear hyperlipemic serum and will prevent the development of or reduce the extent of atherosclerosis in cholesterol-fed animals. A trial of heparin in the treatment of diabetic retinopathy had at least temporarily encouraging results, particularly in cases in which recently and rapidly forming macular plaques were causing progressive deterioration of vision. However, there was a tendency to exacerbation of the lesions after treatment was discontinued.

Considerable interest has been shown recently in the possibility of controlling the progression of diabetic retinopathy and nephropathy by means of hypophysectomy or adrenalectomy. Kinsell [56] stated:

> Because of the production, directly or indirectly, by the pituitary of excessive amounts of "anti-insulin factors," optimal control is clinically impossible in some diabetics. In patients in this category in whom vascular disease is progressing rapidly, hypophysectomy (and possibly adrenalectomy) may decelerate or halt the progress of the vascular disease.

Luft, Olivecrona, and their associates § have now reported the results of hypophysectomy in 20 diabetics. Seven died within 1 day to 19 months after the operation. Twelve of the surviving patients have been followed for 3 to 43 months, but only two of them for more than a year. All but one have normal capillary fragility, and the renal disease has not progressed. The postoperative changes in the retinal lesions are described in some detail, but they are summarized by the statements:

> In all cases save one, except for occasional retinal hemorrhages, no symptoms or signs of progression of the diabetic retinopathy were evident. . . . On the contrary, improvement in visual capacity and/or eyeground changes were noted in most cases.

Kinsell and his associates [67] report similar results following hypophysectomy in five diabetics.

Results of adenalectomy in diabetics with progressive vascular disease are reported by Wortham and Headstream,[68] Martin and Wilson,[69] and Headstream and Wortham.[70] Headstream and Wortham noted improvement of the retinopathy in six of seven patients, with associated improvement of vision in four of them. One of their eight patients had had both eyes removed because of painful secondary glaucoma. Three of their patients had died at the time of their report—one four and a half months, and the others eight months, after operation. These authors state:

> It appears that if adrenalectomy is to be successful it should be done early in the arteriolar degenerative process and the results suggest that in well-selected patients it is a relatively practical and helpful therapy.

An editorial [71] in the *British Medical Journal* comments that hypophysectomy for the complications of diabetes is apparently more hazardous than it is in cases of malignant disease, partly because of the state of the arteries and partly because of the metabolic problems involved. Surviving patients "failed to show any dramatic improvement, but the progress of the complications does seem to have been slowed or actually arrested." The writer concludes that, though removal of the pituitary is obviously a desperate measure, the evidence justifies further investigation, since nothing else at present offers any hope. Also, in an editorial, Sprague [72] comments that the rationale for the treatment of diabetic retinopathy and intercapillary

§ References 65 and 66.

glomerulosclerosis by extirpation of the pituitary or adrenal glands is not entirely clear or well established. He states:

> It is to be hoped that some day a better understanding of the pathogenesis of the degenerative complications of diabetes will lead to methods for their prevention. In the meantime . . . in selected otherwise hopeless cases exploration of such radical treament as hypophysectomy and adrenalectomy seems to be justified. The results to date must be viewed with conservatism, and the studies must be regarded as being in the field of clinical investigation of an illness for which there is no known effective method of treatment.

Lipemia Retinalis.—Adlersberg and Wang [73] found lipemia retinalis in one of five cases of idiopathic hyperlipemia associated with mild diabetes. In a case of lipemia retinalis in diabetes mellitus reported by Haymond and Berry,[74] the hyperlipemia was considered to be of the essential type, since it responded to a low-fat diet but not to control of the diabetes. In a patient observed by Ericson,[75] the lipemia retinalis disappeared in three weeks, although the serum was still milky in appearance and the lipid values were still high. The phospholipid-total lipid ratio is supposed to be of decisive importance in the maintenance of a clear serum. In this case, however, the ratio was the same when the eyegrounds were markedly lipemic and when the blood appeared to be of normal color in the retina.

HYPERTENSIVE DISEASE

From his study of the ocular fundi in 113 patients with essential benign hypertension, Fischer [76] reaches the rather questionable conclusion that there is no characteristic fundus picture in this condition. He thinks that the retinal vessels were normal in 95 of the 113 cases. After critical evaluation of the glyceryl trinitrate flicker-fusion test, Scher and Spankus [77] conclude that "much more work of a basic nature needs to be done before variations in critical fusion value under the influence of nitroglycerin or other drugs may be reliably applied in clinical evaluations of medical conditions such as hypertension." Joyce [78] comments:

> Prognosis in vascular hypertension based on the fundus picture alone has ceased to be reliable since methods of treatment have so greatly improved and since the apparent increase in the number of young cases in which fundus changes are minimal. . . . Some years ago the presence in the fundus of hemorrhages, exudates and papilledema emboldened the ophthalmic consultant to make a definite prognosis. This, alas, no longer holds good.

In Joyce's opinion, in the future, the prognostic value of the retinal lesions will depend on the possibility of establishing a relationship with some other factor or factors in hypertensive disease. He has not been able to do this yet. Bernsmeier, Sack, and Siemons [79] found that there is no significantly prognostic correlation between the state of the retinal vessels and the possible occurrence of acute cerebrovascular disturbances in the hypertensive subject.

Puig Solanes, Quiroz, and Barrientos [80] correlate the clinical retinal and the necropsy findings in 40 cases of essential hypertension, 40 cases of chronic glomerulonephritis, and 10 cases of hypertension secondary to miscellaneous diseases, such as diabetic glomerulosclerosis, pyelonephritis, adrenal cortical adenoma, and pheochromocytoma. They note that the ocular pictures of patients who die of essential hypertension are qualitatively identical with those of patients who die of chronic glomerulonephritis. The "edematous" lesions are more intense in the latter. Renal insufficiency does not correlate with the intensity of the retinal lesions, which depend on the diastolic hypertension. If arteriolar necrosis is used as the diagnostic criterion of malignant hypertension, the retinal pictures are the same in severe nonmalignant and in malignant hypertension. Retinal and cerebral

vascular scleroses are not correlated in intensity, but the retinal and renal forms are correlated. There is also a moderate correlation between retinal arteriolar sclerosis and hypertrophy of the heart.

Bailliart [81] also notes that the state of the retinal vessels does not always, or very faithfully, reflect that of the cerebral vessels. In his opinion the report of the ophthalmic consultant is incomplete unless it includes the retinal arterial pressure. If the ratio of the retinal to the brachial diastolic pressure is 0.45, the hypertension is compensated. A higher ratio indicates an exacerbation of the hypertensive disease. A unilaterally lowered ratio may indicate thrombosis of the carotid artery; a bilaterally lowered ratio may be a premonitory sign of cerebral thrombosis.

Bedell [82] discusses various features of the retinal lesions in hypertensive disease. He notes that the most important retinal sign in toxemia of pregnancy is spasm of the arterioles. If the spasms increase in number and frequency, the pregnancy should be terminated. Kyrieleis [83] also considers the functional change in the vascular system to be the fundamental disturbance underlying the retinal changes in toxemia of pregnancy. Increase in the severity of the retinal vascular changes and the development of changes in the retina itself indicate threatened exacerbation of the other symptoms of toxemia.

Surgical Treatment of Hypertension.—Joly and his co-workers [84] report that retinopathy of Grade 3 or Grade 4 type (without and with edema of the disc) regressed completely in 29 of 35 cases after extensive sympathectomy. Severe retinal lesions do not contraindicate surgical treatment but actually may in themselves necessitate operation for the prevention of blindness. The favorable results are more consistent, more rapid, and more lasting than those obtained by any other form of treatment. Zintel and his co-workers [85] also report improvement in retinopathy following sympathectomy, and they state that data regarding survival indicate that thoracolumbar sympathectomy does improve the life expectancy of the patient. Huntington and Evans [86] compare the survival curves of a group of sympathectomized patients and a group of patients treated medically before the introduction of the ganglion-blocking drugs. Of 147 sympathectomized patients with Grade 3 hypertension, 67% were alive at the end of 5½ years, and 46% were alive at the end of 10½ years, as compared with 20% and 0%, respectively, of the medically treated group. Of 42 sympathectomized patients with Grade 4 hypertension, 43% were alive at the end of 5½ years and 33% at the end of 10½ years, as compared with 5.6% and 0%, respectively, of the medically treated group. The authors state:

> To us, it seems that the patient with hemorrhagic eye grounds and rapidly rising diastolic pressure, with or without coincidental papilledema, who is still young and who still has good kidney function, whose prognosis is statistically grave, with one to four years' life expectancy, is offered most by splanchnicectomy, then a low sodium diet if that is found necessary in subsequent months and then the addition of drug therapy.

Cartier [87] found that in general the beneficial effects of Smithwick sympathectomy were increased by the addition of subtotal adrenalectomy. Retinal lesions improved in 53% of the cases in which the Smithwick method was used and in 90% of those in which additional subtotal adrenalectomy was done. The papilledema receded in all of the three surviving patients with malignant hypertension reported by Revell and his co-workers.[88] But the retinopathy decreased in grade in only 46% of the patients submitted to adrenal resection and sympathectomy by Jeffers and his co-workers.[89]

Medical Treatment of Hypertension.—Satisfactory regression of retinopathy during the treatment of hypertensive disease with various of the newer antihypertensive drugs, especially hexamethonium and pentolinium tartrate (Ansolysen), has been reported by a number of authors, including Agrest and Hoobler [90]; Burnett and Evans [91]; Brunner, Altmann, and Schindel [92]; Doyle [93]; Goldsmith, Beaven, and Lambert [94]; Markovitz, Koik, Hick, and Grissom [95]; Platt [96]; Rast, Orgain, Muller, Pryor, and Sieber [97]; Schroder,[98] and Šimková and Zahn.[99]

Ashby, O'Neill, and Maclean [100] state that, as compared with other reported series, the improvement of vision obtained in their group of cases was disappointing, although in the early stages of treatment of malignant hypertension it was occasionally remarkable. Retinopathy cleared completely in 7% of their cases and was improved but still present in 31%. Blurring of vision due to paralysis of accommodation developed in 19% of their patients. It was treated with physostigmine and, after stabilization of the dosage of pentolinium tartrate, by change of glasses. Hughes, Dennis, and Moyer [101] state that retinopathy improved in only 1 of 5 patients treated with reserpine and hydralazine and in only 3 of 10 treated with reserpine and hexamethonium.

Bruce [102] observed the sudden onset of blindness in a woman, aged 34, with retinopathy of hypertension Grade 3, following the intramuscular injection of 6 mg. of hexamethonium. The blood pressure dropped in four minutes from 260 systolic and 160 diastolic to 180 systolic and 110 diastolic. Bruce thinks that the loss of vision in this case was almost identical with that sometimes produced by systemic collapse or by exsanguination or both. The exact mechanism of the loss of vision was not explained.

Pheochromocytoma of an Adrenal.—Maeder and Forni [103] observed retinopathy with edema of the discs in a 6-year-old boy with persistent hypertension. Three months after the removal of two tumors from the left adrenal there were only slight residuals of the macular stars. The retinal lesions did not differ from those seen in essential or in renal hypertension.

RETINAL VASCULAR OCCLUSIONS

Jaeger and Schoenknecht [104] compared the frequency of retinal vascular occlusions during the years 1946 to 1953 with that in the years 1928 to 1935 and concluded that there has been an extraordinary increase in their occurrence since World War II. They did not explain this increase, since new etiologic factors were found only in exceptional cases. Anderson and Vallotton [105] recommend treatment for all arterial occlusions seen within the first week, and for all venous occlusions seen within the first month, after onset. Anticoagulant therapy is advised for both arterial and venous occlusions. The authors are not convinced that the retinal vessels can be dilated by drugs or by stellate-ganglion block. Improvement was noted in 35% of the treated arterial occlusions and in 50% of the treated venous occlusions, as compared with 5.4% and 13.6%, respectively, in the untreated cases.

Arterial Occlusions.—Hollenhorst, Svien, and Benoit [106] produced the typical picture of closure of the central artery of the retina with rapid progression to optic atrophy in a monkey by pressure on the eye combined with lowering of the systemic blood pressure. Kabakow, Van Weimokly, and Lyons [107] report the occurrence of closure of both central arteries in a patient with cortisone-treated systemic lupus erythematosus, sickle-cell trait, and active pulmonary tuberculosis.

They think that lupus was the most likely cause of the occlusion, though the closure could have been due to either of the other systemic diseases or to the cortisone therapy.

By electroretinographic studies controlled with electroencephalograms, Popp [108] determined that the rabbit retina can regain its full function after 15 minutes of ischemia, can regain partial function after 30 to 75 minutes of ischemia, and can make a delayed recovery after 60 to 90 minutes. After 105 minutes of ischemia, no signs of function can be elicited. Both Weerekoon [109] and Hummelt [110] think that an element of spasm is present in most, if not all, cases of occlusion of the retinal arteries of whatever cause and that vasodilator therapy should be continued for at least three to four weeks in order to obtain the best possible end-result. They recommend tolazoline (Priscoline) as the drug of choice in the early stages of the treatment. Marsico [111] used a hexamethonium preparation in the treatment of six cases of central retinal artery occlusion and obtained improvement in all cases except one, in which the angiospastic factor was associated with severe anatomic changes in the vessel walls.

Temporal Arteritis.—The classic ophthalmoscopic picture of occlusion of the central retinal artery was present in only 1 of the 12 cases of temporal arteritis reported by Meadows.[112] The usual findings were slight or moderate papilledema with a few peripapillary hemorrhages in the early stages and, after some weeks, optic atrophy. The loss of vision in these cases is ascribed usually to lesions in the ophthalmic arteries or in the central retinal artery before it enters the optic nerve. But Meadows thinks that involvement of the short ciliary arteries as they take part in the formation of the arterial circle of Zinn around the nerve head may be the responsible lesion. Meadows treated only three of his patients with cortisone, and the results of the treatment were not satisfactory. There was slight improvement in the vision of one eye of one patient. But one of the patients with normal vision developed sudden bilateral blindness 11 days after cortisone therapy was started. Evans || states, however, that his experience with corticotropin in the treatment of temporal arteritis indicates that marked improvement in vision can be obtained as long as light perception is present. Because serious deterioration is apt to occur soon after the discontinuance of corticotropin, it may be necessary to give a maintenance dose for a long period to prevent the return of blindness.

The description of the ophthalmoscopic findings given by Rizzini and Frassineti [113] suggests that unilateral closure of the central artery of the retina occurred in their case of temporal arteritis. The ophthalmoscopic picture of ischemic optic neuritis was present in the involved eyes of the patients reported on by Griepentrog [114] and by Schwab and Sochor.[115] The latter authors state that the treatments used, including cortisone and corticotropin, have not improved vision and do not usually prevent involvement of the second eye in primarily unilateral cases.

Venous Occlusions.—Palich-Szántó [116] describes a peculiar disc-like formation which developed in the central retina as a late sequel of thrombosis of the central vein. Della Porta [117] studied the serum proteins in 12 cases of closure of the central retinal vein and found a constant low level of albumin, an occasional increase of α- and β-globulins, and a regular increase of γ-globulin. Gasparri [118] found that the prothrombin levels were above normal and the blood pressure was elevated in the majority of 50 cases of thrombosis of the retinal veins.

|| Evans, J., in discussion on article by Meadows,[112] pp. 36-37.

Rintelen and Saubermann [119] state that the fact that, in closure of the central retinal vein, the bleeding is not more extensive than it is commonly, leads to the assumption that there must be a means of outflow for the blood which is brought into the eye. Since the capacity of the anastomoses between the retinal and the choroidal vessels and their connections with the vascular sheath of the optic nerve is inadequate, at least at first, it is probable that the outflow takes place through the central vein itself. The use of anticoagulants is indicated to keep this channel open. Appelmans and Lamotte [120] could not demonstrate increased coagulability of the blood in 15 cases of thrombosis of the retinal veins. They conclude that this physiopathologic factor only rarely plays a part in the production of the thrombosis. Seventy-two per cent of their patients had hypertension and arteriosclerosis. They tried anticoagulant therapy in 10 cases of obstruction of the central vein. Favorable results were observed in three cases of partial thrombosis, in which the anticoagulants seemed to prevent complete obstruction. On the whole, in their opinion, anticoagulant therapy seems not to improve appreciably the visual prognosis in cases of thrombosis of the central retinal vein. They preferred treatment with vasodilators, rutin, ascorbic acid, and adrenochrome (Adrenoxyl). Montagne [121] thinks that in the treatment of retinal venous thrombosis anticoagulants should be combined with vasodilators and with agents to combat capillary fragility. In his opinion, while treatment should be started as soon as possible, it is worth while to try anticoagulants, even several weeks after the onset. He obtained good results from treatment in two cases in which the treatment was started two weeks and eight weeks after onset, respectively. Hentschel [122] thinks that in venous, as well as in arterial, circulatory disturbances in the retina the most important factor is an angiospastic reaction, and that the best treatment for retinal venous thrombosis is intravenous Eupaverine (methylenedioxynbenzylmethylmethylenedioxyquinoline).

Birge [123] calls attention to the advisability of checking the blood volume in patients with thrombosis of the retinal veins. He states that he has found low-grade polycythemia in 22 cases of retinal venous thrombosis, and that improvement has been obtained more frequently by normalizing the blood volume than by the use of anticoagulant drugs.

CHORIORETINITIS IN TOXOPLASMOSIS

Toxoplasmosis seems to be assuming an increasingly important position among the causes of uveitis, particularly the posterior variety (chorioretinitis). Frenkel ¶ states that, in the experimental animal, the organisms and lesions are primarily in the retina and that the changes in the choroid and in the anterior segment are secondary. Hence uveitis appears to be secondary to retinitis, and the toxoplasmic etiology of iridocyclitis must be doubted. A dual etiology of lesions is to be expected in humans, as in animals. There are two forms of Toxoplasma, proliferative and cyst. The proliferative forms destroy cells and cause tissue necrosis. They are inhibited by chemotherapy, but cortisone aggravates the tissue lesions. When a cyst ruptures, a lesion of hypersensitivity results. This type of lesion can be controlled by cortisone or corticotropin, but chemotherapy should be given at the same time, since proliferative forms of Toxoplasma may be present also. Frenkel [124] also states that in experimentally induced Toxoplasma infections in hamsters, eye lesions appeared sporadically, and after months of infection.

¶ Frenkel, J. K., in discussion on article by Ryan and others,[124] pp. 879-882.

Siegert # discusses in considerable detail the value of serologic tests for the diagnosis of toxoplasmic and other infections of the eye. In general, positive tests do not prove that the eye lesion is caused by the systemic infection, and negative tests do not necessarily exclude the infection from consideration as the possible causative factor.

Congenital Toxoplasmosis.—Holmdahl and Holmdahl [127] state that half of all newborn infants can be expected to have antibodies against Toxoplasma with dye-test titers between 1 : 10 and 1 : 8000. In the majority of cases this results from passive immunization acquired during intrauterine life. In the passively immunized child, the antibody titer falls to less than 1 : 250 during the first six months of life. During a four-year period it was possible to establish only 2 definite and 1 probable case of toxoplasmosis among 23,260 infants born alive who have been followed up to the age of 3 to 6 years. Nathan and Matheson [128] report two cases of infantile toxoplasmosis; in one of them chorioretinitis was present. The authors state that, when a high dye-test titer is obtained in an infant during the first weeks of life, a complement fixation test should be done on the mother and on the child. If, in addition to a positive dye test, the mother has complement-fixing antibodies and the child does not, this is indicative of an active infection, which should be treated. Mehta [129] reports two cases of chorioretinitis due to congenital toxoplasmosis. In both the patient was a first child, and the second child in each instance was normal. This suggests either that the parasitemia is transitory during pregnancy or that neutralizing antibodies are formed quickly in the maternal blood, so that further calamity is avoided.

Ariztia, Martinez, Howard, and Latorre [130] observed bilateral acute macular chorioretinitis in an infant from whose spinal fluid they were able to isolate Toxoplasma. Habegger [131] was able to demonstrate Toxoplasma in the spinal fluid and in the aqueous of a 2-month-old infant who had chorioretinitis and hydrocephalus.

Adult Toxoplasmosis.—Habegger [131] found Toxoplasma also in the subretinal fluid removed by puncture from the eye of a 45-year-old woman who had multiple foci of chorioretinitis and detachment of the retina. The aqueous fixed complement in a dilution of 1 : 16. In a study of the etiology of uveitis, Smith and Ashton [132] found a striking association between Toxoplasma infection and posterior uveitis and between raised antistreptolysin titers and anterior uveitis. Rougier and Garin [133] discuss the diagnosis of ocular toxoplasmosis and report 12 cases, 3 of juxtapapillary and 3 of disseminated choroiditis, 3 of uveitis, and 3 of iridocyclitis.

According to Ryan and his co-workers,[134] the presumptive diagnosis of toxoplasmosis in a case of uveitis is made by the correlation of all available significant data: clinical appearance, absence of more convincing evidence of other etiologic possibilities, the presence of skin sensitivity to toxoplasmin, and the presence of anti-Toxoplasma antibodies, as revealed in the dye test. No particular dye-test titers are accepted as diagnostic. Sixty-seven cases of granulomatous uveitis were investigated. The diagnosis of acquired toxoplasmosis was made in 37 and of congenital toxoplasmosis in 2. Posterior uveitis was present in 34 of the 39 cases; there was associated anterior uveitis in 9 cases. The 29 patients who had active lesions were placed on doses of pyrimethamine (Daraprim) and sulfonamide drugs, chiefly sulfadiazine. Satisfactory clinical evidences of improvement were

References 125 and 126.

noted in 25 cases—in 8 within a week after the institution of treatment. Toxic reactions were frequent, especially intermittent nausea with occasional vomiting, anorexia, and loss of weight. Disturbances in the hematopoietic system were noted in about one-fourth of the patients, but recovery was rapid when the dose was reduced or the drug stopped.

Cassady, Culbertson, and Bahler [135] performed methylene blue dye tests on the sera of 36 patients with vascular or inflammatory disease of the posterior uvea; 23 sera were positive for toxoplasmosis. No other cause could be found in these cases. In the 16 cases with active lesions, the dye test was positive in titers of from 1:64 to 1:512. There was marked and dramatic improvement in the uveitis in 11 patients who were treated with pyrimethamine and sulfadiazine. The authors stated that, since this treatment is potentially dangerous, it should not be used unless the leucocyte and platelet counts can be followed carefully.

TREATMENT OF TUBERCULOUS LESIONS OF RETINA

Mitchell [136] suggests for the treatment of ocular tuberculosis long-term and sustained chemotherapy with isoniazid, streptomycin, and aminosalicylic acid U. S. P. in the manner employed in the treatment of renal tuberculosis. Kratka [137] concludes from his experimental studies that isoniazid is a relatively nontoxic agent and that it can be administered safely over prolonged periods, with only rare and preventable side-effects. It displays definite bacteriostatic, and possibly bactericidal, properties in the treatment of tuberculous ocular lesions in nonimmune, nonallergic rabbits. It has a more rapid and more effective therapeutic value than streptomycin or aminosalicylic acid. Sutton and Beattie [138] report a case in which a bilateral toxic optic neuritis followed by optic atrophy, with permanent reduction of vision to 4/60 and 3/60, was caused apparently by isoniazid. They think, however, that there must have been an idiosyncrasy to the drug, since toxic neuritis due to isoniazid in the dosage used had not been reported previously.

Lebensohn [139] and Montouroy [140] report good results in the treatment of lesions of the posterior segment of the eye with combined isoniazid, streptomycin, and aminosalicylic acid. Payrau, Guyard, and Perdriel [141] treated eight patients who had different types of uveitis of almost certain tuberculous etiology with isoniazid alone. Complete cure was obtained in five of six cases of chorioretinal lesions. Cicatrization of the nodular lesions occurred after two months' treatment, on the average.

Riehm [142] defined focal ocular tuberculosis as a hematogenous metastasis in which bacilli are seeded in the eye but do not multiply there (abortive metastasis). In his opinion, chemotherapy is superfluous in this type of eye lesion, since the drugs are only bacteriostatic, and will not affect bacilli which are already nonvirulent and not capable of multiplying. He advised immediate rest in bed, an optimal diet with added vitamins, and heat to the eye. Resorption of the focus in the retina takes five to eight weeks. Chemotherapy should not be considered until this period has elapsed.

Recurrent Hemorrhages into the Vitreous.—Seidel [143] found all blood studies normal in 20 male patients between the ages of 17 and 49 with typical retinal periphlebitis, and the sedimentation rate was normal in 19 of the 20. Elliot [144] considered Eales' disease as a clinical entity, and not as a manifestation of many disease conditions. In his opinion, the hemorrhages and exudation result from a hypersensitivity reaction in the venous wall in persons who have been sensitized

to tuberculoprotein. Eight of his patients had active or healed pulmonary tuberculosis, and the skin tuberculin test was positive in 30 of his 31 patients. In Elliot's opinion, chemotherapy has not been uniformly beneficial in this condition. Rest in bed is important for one or two weeks when fresh bleeding occurs. Tuberculin therapy did not prevent recurrence of the hemorrhages. X-ray therapy is of doubtful value. Diathermy coagulation was not successful in the one case in which it was tried. Further hemorrhage did not occur under observation in three patients who were given cortisone or corticotropin for prolonged periods.

Kratka [137] noted improvement in 11 of 16 cases of periphlebitis with hemorrhages during treatment with isoniazid. In his opinion, isoniazid therapy must be continued for two to four weeks before clinical improvement can be expected, and it must be continuous for a minimum of four months to obtain a clinical cure. He favored the addition of cortisone to the isoniazid therapy. Velický [145] also noted improvement in 9 of 14 cases of retinal periphlebitis under treatment with isoniazid. But these patients were treated in an institution for the climatic and hygienic care of ocular tuberculosis, and, in Velický's opinion, the improvement was due to this care. He recommends this method of treatment instead of drugs for the types of ocular tuberculosis with bleeding. Relapses are not prevented by chemotherapy.

Hoffmann [146] treated 202 cases of hemorrhage into the vitreous, including 60 associated with periphlebitis, by irradiation. Treatment of 136 was with radium and of 66 with x-rays. Great clearing of the vitreous was obtained in nearly all cases. Various residuals in the retina prevented good end-results from the standpoint of vision in a number of cases. In 26 cases in which the disease had continued for many months or more than a year, progressive clearing took place after the beginning of radiation therapy. This suggested that the improvement was due to the treatment and was not a spontaneous chance occurrence. Full vision was recovered in 42 of 98 eyes with periphlebitis.

THE RETINA IN VARIOUS SYSTEMIC DISEASES

There are retinal manifestations of so many and so varied systemic diseases that it is possible only to mention them briefly. Mattsson [147] observed recurrent retinitis in a case of Reiter's disease. Malatesta [148] states that the fundus picture of an 11-year-old girl with Niemann-Pick disease resembled that of amaurotic familial idiocy, except that the disc was not as atrophic and the zone around the red spot in the macula was grayish-blue instead of shiny-white. Falls and his coauthors [149] note that the presence of retinal periarteritis with or without associated extensive, dense, sheet-like hyaline opacities in the vitreous in the absence of inflammation of the anterior segment should suggest the possibility of hereditary primary systemic amyloidosis, especially if the patient has widespread bizarre symptoms. Scott, Friedmann, Chitters, and Pepler [150] and Krümmel and Rausch [151] call attention to the frequent involvement of the eyes in the syndrome of incontinentia pigmenti, often in the form of pseudoglioma. They describe the histologic findings in the eyes of their patients. Each had complete detachment of the retina with a connective-tissue membrane between the anterior surface of the retina and the posterior surface of the lens. Givner [152] observed an elevated mass in the macula of a patient with malignant lymphoma. At necropsy, this proved histologically to be a subretinal transudate associated with marked thickening of the lamina vitrea, which was suggestive of a degenerative lesion.

Blood Dyscrasias.—Straub and Goldeck [153] observed in two pregnant women preretinal hemorrhages which cleared after the correction of an iron-deficiency anemia. Davies [154] describes lipemia retinalis in a patient with xanthoma eruptivum and enlargement of the spleen. In a woman with reticulosarcomatosis, Leonhardt [155] found in the retina hemorrhages and white patches with hemorrhagic borders, which he thinks were associated with acute anemia, thrombocytopenia, and increased capillary fragility. Danis, Brauman, and Coppez [156] and Clarke [157] describe the dilatation, tortuosity, and irregularity of the retinal veins with hemorrhages in the retina and the fragmentation of the blood stream in the veins on compression of the globe which results from the increase in plasma proteins, and often associated cryoglobulinemia, in cases of multiple myeloma. Clarke notes also that paralyses of ocular muscles may be caused by involvement of the nerves at the base of the skull by plasma-cell myeloma.

Caselli [158] observed choked discs, retinal hemorrhages, and weakness of the left lateral rectus muscle in a case of purpura haemorrhagica. As the cause of the blurring of vision which was the first subjective symptom of a patient with polycythemia, Bech [159] found obstruction of a tributary retinal vein with extensive hemorrhage in the retina. In a young woman with a hemolytic constitution, Otto [160] observed a peculiar segmental pigmentation of the retina in each eye, with corresponding defects in the visual fields; these he thinks were due to the absence of nerve fibers, which could be detected by examination of the fundus with red-free light. There were numerous other congenital abnormalities. Alfano and Roper,[161] Unger, [162] and Comberg [163] discuss and report cases of loss of vision following blood loss.

Collagen Diseases.—Segal [164] describes the physiology of the connective tissue and the histologic changes that occur in it during the course of the collagen diseases and discusses the associated eye disturbances. Godtfredson [165] divides the acute collagen diseases into three groups according to the location of the main symptoms in the joints, in the skin and mucous membranes, or in the vascular system, and outlines the ocular lesions which may be expected in each of these groups. He includes temporal arteritis among the manifestations of the vascular group. In his opinion, the eye signs represent an allergic-hyperergic tissue reaction, which responds favorably to treatment with cortisone and corticotropin.

Clifton and Greer [166] describe the clinical, ophthalmoscopic, and pathologic findings in two fatal cases of acute systemic lupus erythematosus. Histologically, they found edema of the retina, cytoid bodies, and hemorrhages in the nerve-fiber layer of the retina, shallow detachment of the retina, degeneration of the rods and cones, and mild round-cell infiltration of the choroid. They state that the precise nature of the cytoid bodies is not known, but that, in their opinion, the cardinal factor in the pathogenesis is damage to the capillary endothelium, which increases permeability and permits escape of plasma and red cells into the nerve-fiber layer. This capillary damage may result from circulating toxins, anoxemia, or stagnation in the capillary bed from obstruction to arterial supply or to venous outflow.

Duguid [167] states that periarteritis nodosa may affect the eyes by involving any of the arteries or by causing hypertension and its resultant retinal lesions. He presents histologic sections supporting his contention that the lesions of periarteritis are due to the lodgment of emboli. Laje Weskamp and Segura [168]

observed the development of arteriospastic retinitis and a profuse hemorrhage into the anterior chamber during the late stages of a case of periarteritis nodosa of predominantly cutaneous type.

Degeneration of Elastic Tissue.—McWilliam [169] agrees that primary angioid streaks result from degeneration of the elastic tissue of the lamina vitrea of the choroid, with resultant loss of transparency and anatomic defects in the membrane. But he calls attention to a secondary type resulting from the accumulation of pigment in local lesions, such as detachment of the choroid and retinal folds. Brand, Kádas, and Arató [170] report a case of the Grönblad-Strandberg syndrome in which there were advanced fundus changes with hemorrhages and in which lesions of the elastic tissue in the skin, and especially in the vessel walls, were demonstrated histologically. In their opinion, these elastic-tissue lesions are part of a generalized weakness of the connective tissues, which is evidenced clinically by increased permeability of the walls of the choriocapillaris with hemorrhages and subsequent extensive scar formation. Rizzuti [171] describes the steady progression over a period of 27 years of the hemorrhagic macular lesions in a patient with angioid streaks and pseudoxanthoma elasticum. Voisin and Lombard [172] observed bilateral macular degeneration with surprisingly good vision in a case of pseudoxanthoma elasticum in which there were no angioid streaks. Thomas, Cordier, and Algan [173] describe in the fundi of a patient with the Ehlers-Danlos syndrome (hyperelasticity and fragility of the skin, hyperlaxity of the joints, and molluscoid tumors of the skin) thinning of the retinal pigment epithelium and the lamina vitrea in the preequatorial region with irregular pigmentation and circumscribed clear, white patches, which were interpreted as breaks in the lamina vitrea. They state that the Ehlers-Danlos syndrome and the Grönblad-Strandberg syndrome with angioid streaks might be present in the same person.

Unusual Vascular Diseases.—Currier, DeJong, and Bole [174] found optic atrophy in one eye and visible blood stream in both retinas in a case of pulseless disease. Leo [175] describes caliber irregularities, fragmentation of the blood stream, and arteriovenous short circuits in the retinas and lens opacities in two cases of pulseless disease, which was diagnosed as endangiitis obliterans in one and as mesaortitis in the other. In a patient who died with left hemiplegia resulting from noninflammatory thrombosis of the right common and internal carotid arteries, Müller [176] found progressive retinal perivasculitis with exudations and proliferations. Histologic examination revealed massive lymphocytic inflammation of the entire vessel wall with severe narrowing of the lumen of some of the vessels.

Dufour and Welter [177] describe multiple foci of retinal periarteritis with a few petechiae in the retina and some small whitish foci in the choroid in a patient with the clinical picture of generalized polyarteritis of unknown origin. Rosselet [178] observed bilateral loss of vision in two cases of temporal arteritis, proved by biopsy, and sudden loss of vision of the right eye of a patient with a syphilitic aneurysm of the aorta and lowered pressure in the right brachial artery. The author states that the experiences of others with pulseless disease and his personal experience with a patient with generalized occlusive vascular disease suggest that the relative lowering of retinal arterial pressure of whatever cause can produce ocular lesions similar to those seen in temporal arteritis.

Davenport [179] calls attention to the frequent association of retinal vasculitis with recurrent hemorrhages into the retina and vitreous with anterior uveitis, occurring at the same time or in different episodes. The cause is unknown; an

association with lesions in the central nervous system has been noted. Friemann [180] observed transitory infiltrates on the walls of the retinal arteries or veins in several cases of uveitis. He interprets them as representing an allergic reaction of the vessel wall.

Fotopulos and Heidrich [181] diagnosed thrombosis of the internal carotid artery in the absence of other specific clinical findings on the basis of the presence of blindness with edema of the macula in the homolateral eye, dilatation of the homolateral sphenoparietal sinus, and dilatation of the frontal branch of the contralateral temporal artery. The diagnosis was confirmed at necropsy. Brændstrup [182] states that the retinal vessels are dilated, tortuous, and dark in color in cases of congenital heart disease with cyanosis but are normal, except for the occasional presence of sclerosis of the vessels, in cases without cyanosis. In cases of coarctation of the aorta, the retinal arteries show regular undulations in the plane of the retina; but, in spite of severe and persistent hypertension, the retinal arterioles rarely are sclerosed, and hemorrhages and transudates do not occur. Retinal arterial pulsation may be increased.

Under the general heading of disorders of the autonomic nervous system, Koch [183] discusses migraine, amaurosis fugax, central angiospastic retinopathy, commotio retinae, Raynaud's disease, and thromboangiitis obliterans. In his opinion, amaurosis fugax results from angiospasm secondary to cardiovascular irritability in young persons and to organic vascular disease elsewhere in older persons. This condition must be distinguished from central angiospastic retinopathy, in which spasm of the smaller arterioles in the macular region due to autonomic instability results in capillary disturbance and edema in the macular retina.

Contagious and Infectious Diseases.—Palich-Szántó and Valér [184] discuss the importance of certain previously unrecognized signs—indistinct disc margins, development of connective (not glial) tissue in the physiologic cup, and perivasculitis—in the diagnosis and estimation of the activity of completely asymptomatic cases of syphilis with positive spinal fluids.

In a case of infectious mononucleosis, Jones [185] observed retinal and subhyaloid hemorrhage, which he ascribed to periphlebitis in the central retinal vein, since there were three focal areas of perivascular cuffing in the retina. These areas disappeared in two weeks, but it took six months for the subhyaloid hemorrhage to be completely resorbed.

Choyce [186] states that he has not seen a chorioretinal lesion which could be attributed to leprosy rather than to some intercurrent disease. The mycobacteria can be demonstrated readily histopathologically in the ciliary body and occasionally in the anterior part of the choroid, but not in the retina. Kirwan [187] agrees with these statements in general but adds that lesions of the posterior segment of the eye back of the ora serrata do occur occasionally by direct spread from lesions in the anterior segment. Amendola [188] states that sulfonamide therapy has an indisputable therapeutic effect on ocular leprosy and also a prophylactic effect, so that ocular involvement occurs now only when the leprosy is not recognized until it is in the cutaneous-mucosal-visceral stage.

Toulant and Boithias,[189] Weyts,[190] and Budden [191] describe the ocular complications of onchocerciasis and discuss the mechanism of development of the optic atrophy and choroidoretinal lesions which are characteristic of this disease. Recupero [192] noted that 5 of 50 infants and young children with infantile internal leishmaniasis had retinal hemorrhages due to increased vascular fragility, low platelet

count, and prolongation of the prothrombin time. In one case there was partial thrombosis of the central retinal vein, which in his opinion was due to endothelial changes and slowing of the blood stream.

In one of the four cases of trichinosis reported by Edwards,[193] in addition to the usual signs of pain and tenderness over the eyes, chemosis of the conjunctiva, and edema of the lids, there were scattered hemorrhages in the retina around the discs. Jeffery [194] mentions six cases of retinitis and retinochoroiditis associated with Ascaris, six with hookworm, and one with dysentery caused by Endamoeba histolytica.

Diseases of the Nervous System.—Paufique and Etienne [195] report a case of multiple sclerosis with sheathing of the retinal veins. In their opinion, the recognition of perivenous sheathing as a characteristic finding in multiple sclerosis focuses attention again on the possible vasomotor or allergic nature of the disease. Funder [196] found a unilateral Kayser-Fleischer ring in a patient with hepatolenticular degeneration (Wilson's disease). In the eye with the ring there were circumpapillary choroidal atrophy and a circumscribed area of choroidal sclerosis at the posterior pole. In the eye without the ring there was a hypermature cataract. When the cataract was extracted, an old detachment of the retina with thick strands in the vitreous was found. It seemed possible that changes in metabolism in this eye as a result of the detachment might account for the absence of the Kayser-Fleischer ring. The finding of a saccular aneurysm on the superior temporal artery and of varicose dilatations of the retinal veins of the right eye of a woman with progressive syringomyelia suggested to Yourish, Wollin, and Nathaniel [197] that a congenital vascular anomaly of the brain stem and cervical cord might be responsible for the neurologic changes.

In one of the cases of Schilder's disease reported by Nover,[198] bilateral choked disc was present. In the other, there were numerous small elevated white patches in the retina superficial to the retinal vessels. Histologically these proved to be postinflammatory granular and cellular deposits on the internal limiting membrane of the retina, and not glial plaques. Pagenstecher [199] and Meyrán, Kai, and Espinosa [200] describe elevated masses in the retina in cases of tuberous sclerosis.

Moro [201] reports the finding of fundus changes, papilledema, hemorrhages in the retina and vitreous, and spasm of retinal arteries in 86% of 37 cases of subarachnoid hemorrhage, 10 of which were fatal. In his opinion, in cases of subarachnoid hemorrhage without retinal lesions, it can be assumed that there is a small amount of bleeding or else that the site of the bleeding is far removed from the perichiasmatic optic pathways. In one case, histologic examination revealed marked venous stasis in the optic nerve and choroid, papilledema, and hemorrhages in the retina and in the meningeal sheaths of the optic nerve resulting from stasis in the ophthalmic vein, caused, he thought, by increased pressure in the cavernous sinus.

Médinger [202] reports a case of Harada's disease in which the vision returned to normal at the end of 16 months. Lopez Marin [203] reports two cases of the Vogt-Koyanagi syndrome in which there was severe permanent loss of vision and points out the difficulty in differential diagnosis between the Vogt-Koyanagi syndrome and Harada's disease. Cordes [204] states that the weight of current opinion favors the consideration of Harada's disease and the Vogt-Koyanagi syndrome as clinical variants of the same condition but that their relation to sympathetic ophthalmia is more questionable. Swartz [205] reports the apparent precipitation of

a Vogt-Koyanagi syndrome with residual permanent blindness by extracapsular lens extraction. In his opinion sympathetic ophthalmia and the Vogt-Koyanagi syndrome are basically the same entity. In sympathetic ophthalmia the etiologic agent gains entrance to the eye and progresses to the intracranial contents. In the Vogt-Koyanagi syndrome the etiologic agent gains entrance to the brain and progresses to the eye.

RETINAL DETACHMENT

Hertz [206] publishes a monograph dealing with detachment of the choroid, associated detachment of the retina, and resultant pigmented streaks in the retina, which must be differentiated from angioid streaks. Schepens [207] depicts the appearance of the fundus and of the vitreous in two cases of detachment of the macular retina and in two cases of peripheral detachment. Michaelson [208] describes a detachment of the inferior temporal retina associated with a dehiscence and two small holes in the retina. Numerous fine white lines could be seen in the areas of the dehiscence and the holes. Observation over a period of two years showed that these white lines represented sclerosed choriocapillaris, which Michaelson thinks probably played a part in producing the retinal disturbance. François and Verriest [209] present an extensive and detailed study of the visual functions of the detached retina before and after successful replacement. Rathschüler and Dufour [210] suggest that there is a predisposition in highly hypermetropic eyes to vascular lesions and retinal detachments of certain types. Hansen and Stewart [211] observed total detachment of an atrophic retina and subluxation of the lens in a highly myopic 5-year-old child, both of whose parents had myopia and retinal detachments. The authors think that genes for both myopia and cystic degeneration of the equatorial retina were present in the child. From their study of a large series of cases, Huerkamp and Behme [212] formed the opinion that the greater tendency to secondary rise in tension in cases of detachment of the retina with circular and multiple oral tears is explained by the proliferation of pigment epithelium in the detached areas and the resultant blocking of the posterior channels of outflow of the intraocular fluids.

Etiology of Detachment.—Zur Nedden [213] and Gasteiger [214] discuss the various types of injury to the eye, direct and indirect, which can cause detachment of the retina in predisposed or nonpredisposed eyes and the legal implications of trauma in relation to detachments. A study of 1363 unilateral and 221 bilateral detachments by Huerkamp, Leidig, and Klomp [215] showed that in practically all cases there were associated conditions which were considered to be contributory causes of the detachment. In their opinion, their statistics may aid in evaluating cases of possibly traumatic detachments.

Halbron [216] reports four cases in which detachment of the retina with tears developed in association with an unexplained temporary rise in blood pressure. Poos * discusses the pathogenesis of the cystoid spaces in the retina and of intraretinal cystoid transudation and attempts to explain the origin of retinal tears and detachments on the basis of the inherent force of this edematous change and the transudation of an albuminous fluid from the retina into the space between the retina proper and the retinal pigment epithelium. In his opinion, this intrinsic retinal progressive detaching force is of greater importance than the generally accepted vitreous traction and should be considered in the treatment of detachments.

* References 217 and 218.

Keeney [219] states that simple macular holes of the common degenerative type rarely produce true retinal separation, even when they are complete. A hole may develop in the macula as a secondary change in an old idiopathic detachment. Surgery directed to the peripheral tears or disinsertion will result in complete reattachment of the retina if the apparent hole is really a cyst or if the cyst has ruptured through the inner wall only. Klien [220] illustrates three varieties of retinal holes and shows histologic sections of two of the varieties. Holes may form at the actual site of a vitreoretinal adhesion by tearing out of an operculum, in a weakened cystic degenerated retina at some distance from a vitreoretinal adhesion, or by traction from shrinking preretinal membranes in areas where contact between the retina and the vitreous has been lost for a long time.

Prognosis.—Okamura and Schepens [221] state that in cases in which a retinal break is associated with a minimal detachment the probability of a cure by operation is as high as 95%. But if the detachment is allowed to progress, this figure will drop to 50% or 60%, owing to the formation of fixed folds in the retina. Cures have been obtained by scleral buckling in cases which would have been considered hopeless five years ago. François and de Rouck [222] noted that the preoperative electroretinogram is valueless from a prognostic standpoint, since an extinguished electroretinogram does not necessarily indicate an operative failure. In the study of 280 cases of spontaneous detachment, Gemolotto [223] did not find confirmation of the frequently expressed opinion that a detachment that does not respond to preoperative rest has an absolutely unfavorable surgical prognosis.

Results of Surgical Treatment.—Swan and Christensen [224] studied the effects of various techniques of diathermy by applying diathermy to the sclera of viable human eyes during enucleation. They state:

> During the surgery for retinal detachment shrinkage of the sclera may result from diathermy. A discussion of the favorable and unfavorable consequences of this occurrence is beyond the scope of the present report; however, it did seem important to establish the determining factor so that shrinkage can be avoided or obtained in accordance with the surgeon's wish.

Liehn and Schlagenhauff [225] made an extensive statistical study of 300 consecutive cases of detachment treated surgically; 160 (53.3%) were healed in the sense of reattachment with or without improvement of function. Gormaz and Verdaguer [226] obtained good results from lamellar scleral resection combined with diathermy closure of tears in 48 of 62 cases of detachment of over one month's duration. Salgado-Gomez [227] describes the techniques for partial and total (circular) lamellar scleral resection and states that total scleral resection may prove helpful in long-standing extensive detachments which were believed previously to be incurable. Janssens [228] obtained healing or improvement in 60% of 51 cases of retinal detachment by "reefing" or "tucking" of the sclera; all cases listed as healed or improved showed anatomic reattachment and improvement in visual acuity and visual fields.

Surgical Techniques.—Meek [229] asserts that the usual lamellar scleral resection shortens the anteroposterior diameter of the globe but the retina remains on the stretch from side to side. He describes the addition to the usual procedure of a meridional lamellar scleral resection to shorten the side-to-side arc and relieve the tension on the retina in this direction. In six of eight cases operation by this technique was successful, but the detachment recurred in one of these one month after the patient left the hospital. Everett [230] describes a new type of scleral shortening in which the sclera is folded outward. Young [231] reports a case in

which detachment of about three-fifths of the retina was associated with a large equatorial scleral staphyloma. The staphyloma was buckled inward, and diathermy was applied to the detached retina. Reattachment was secured, with a resulting vision of 20/30. Thomassen [232] operated on 75 detachments by the Rosengren method (widespread surface coagulation with injection of air into the vitreous so that an air bubble is apposed to the tear in the retina). Reattachment was secured in 58 of the 75 cases, but recurrence of the detachment occurred in 6 cases within six months. There was massive bleeding into the vitreous in eight cases; this cleared completely in three cases, and the retina was found to be reattached.

Unorthodox Methods of Treatment.—Böhme and Bangerter [233] emphasize the superiority of retrobulbar implantation of amniotic tissue in the treatment of retinal detachments with small macular holes. Dellaporta [234] states that experimental and clinical observations indicate that the shortening of the sclerochoroidal wall seems to be the decisive factor in the success of the scleral resection operation. In a search for other methods of shortening this wall, 0.3 to 0.5 cc. of rabbit's citrated blood was injected into the suprachoroidal space. This caused flat detachment of the entire uvea for two weeks, temporary shortening of the choroid, and permanent increase in the thickness and compactness of the choroid. In cases in which a detached retina is not reducible by rest and perforating cauterization does not reach the retinal tear, Strampelli [235] advises the insertion of a small, compressed gelatin sponge between the sclera and the choroid through a scleral incision. This sponge will swell and keep the previously cauterized choroid in contact with the retinal tear until a firm adhesion is formed. Stimulated by the observation of injuries to the macula in solar retinitis, Meyer-Schwickerath [236] developed a method for coagulating circumscribed defects in the retina by means of light rays under ophthalmoscopic control. He states that this method results in firm adhesion between the retina, choroid, and sclera; it would seem to be applicable particularly in the closure of small holes before the development of extensive detachment of the retina.

Complications and Side-Effects of Surgery.—Boudet and Montagne [237] discuss the appearance during surgical treatment of multiple tears in a detached retina in which preoperatively only a single tear or none was found. In their opinion these tears have been concealed by the detachment itself, and they suggest that, to obtain a successful result, the retina should be reexamined after each coagulation during the course of the operation. Moore [238] observed two small choroidal detachments seven days after a detachment of the retina was operated on by diathermy punctures with free drainage of subretinal fluid. In his opinion they were caused by serous exudation from the choroidal vessels as the result of intraocular hypotension. The retina was found to be reattached eight weeks later. Frey [239] noted more or less well-developed disturbances of the eye muscles in 19 of 54 cases successfully operated on for retinal detachment. He discusses methods for preventing or correcting these muscle involvements.

Frey [240] also reviews the results obtained in 32 eyes in which 42 globe-shortening operations were done successfully for the treatment of retinal detachment, in most cases by full-thickness scleral resection. The refraction remained unchanged in 11 eyes; it was changed 1.75 D. or less in 7, almost without exception in the direction of hyperopia. Twelve eyes showed an increase in hyperopia of more than 2 D., and two eyes became more myopic.

TUMORS OF THE RETINA

Paine [241] discovered bilateral symmetrical retinal cysts in a patient whom he examined because of trauma to one eye. He called attention to the two theories of origin of these cysts; either they represent a congenital developmental defect, or they are an exaggerated form of cystoid degeneration of the retina. He noted also that there is a tendency for these symmetrical cysts to rupture and produce detachment of the retina. Dekking [242] presents photographs of the fundus of a 9-year-old girl in which a greatly distended retinal artery and vein communicated directly in the periphery, and also photographs taken two and a half months later showing reduction in size of these vessels but a new arteriovenous communication above the disc. Three years later the vessels had increased somewhat in size but were still not as large as they had been originally.

Malone [243] defines a diktyoma as a medulloepithelioma which arises from the more highly differentiated part of the retina, the pars ciliaris retinae, and mimics embryonic retina. He observed a case, in which the patient was a 5-year-old child, which demonstrated that these tumors may not be as benign as they commonly are supposed to be; it terminated fatally as the result of intracranial extension. Schimkat and Unger [244] thought an elevated macular lesion that they found in a man with metastatic carcinoma in a supraclavicular lymph node was also a metastasis. But histologic examination of the eye removed at necropsy showed a mass of fibrous tissue between the retina and the choroid which was interpreted as a fibroma. Ryan [245] reports four cases of massive retinal gliosis which he did not attribute to the organization of hemorrhage. In the eyes of two children in which enucleation was done because of suspected glioma, he thought that the lesions arose as a proliferation of mesenchymal cells from the retinal vascular tree and should be designated "massive retinal fibrosis." He considered two similar lesions in adult eyes to be true gliosis arising from Müller's cells. The histologic diagnoses in 11 cases of pseudoglioma examined by O'Day [246] were postinflammatory endophthalmitis, 4; juvenile Coats' disease, 2; cicatricial retrolental fibroplasia, 1; proliferation of fibrovascular tissue from the hyaloid vascular system, 2; congenital encephalo-ophthalmic dysplasia, 1, and massive retinal fibrosis, 1.

Teng and Katzin [247] present evidence from four selected cases of retinoblastoma to show that the nerve cells of the retina in general demonstrate signs of dedifferentiation and retrogression in the presence of retinoblastoma. They conclude that this retinal change is due to an induction factor which is responsible for secondary foci of tumor growth and that this induction factor is "a chemical substance produced by living tumor cells, soluble in vitreous and subretinal fluid, and diffusible through the limiting membrane of the retina." Stallard [248] states that a neoplasm might appear in some part of the fundus remote from the original site as early as two weeks after radiation treatment of the original growth. The ages at which multiple islands, two to five in number, appeared in 26 patients after successful irradiation of the neoplasm varied from 3 to 25 months. However, it is desirable, Stallard advises, to continue follow-up examinations at monthly intervals until the child is 5 years of age; after this time the neoplasm is most unlikely to reappear.

Hereditary and Familial Factors.—Of 15 children with unilateral retinoblastoma reported by Rippstein,[249] 10 survived. One of these patients married 20 years after removal of the affected eye and had three heathly children. Three of

six patients with bilateral tumors survived; all were blind. Of the 21 patients, 13 had 18 siblings; all were healthy. All 21 were "sporadic" gliomas. De Gennaro [250] collected data from 1893 cases of glioma of the retina—18 personal cases, and 1875 cases from the literature. There were 1700 unilateral and 193 bilateral tumors. A familial character was absent in 80% of the cases. The inheritance is usually recessive, he states, and the penetrance is slight, so that several generations can be free of the disease; and, if a glioma does appear after several generations, it may be considered "sporadic." Reese [251] recalls that an analysis in 1949 of several series of unselected cases of sporadic retinoblastoma indicated that the likelihood of a second sibling's being affected is less than 4% and probably nearer 1%. It was concluded, therefore, that parents who had had one child with a sporadic retinoblastoma might be permitted to have more children. (A "sporadic" case is defined as one in which both parents have normal eyes and no relative of the child has had retinoblastoma.) Retinoblastoma developed in 77% of the children of parents one of whom had survived a retinoblastoma. Of the 15 families analyzed, there was only one in which all three children were free of the disease. Therefore, a survivor from retinoblastoma should not have children.

Palomino Dena and his co-workers [252] publish an extensive analysis of their observations on 82 patients with retinoblastomas involving 100 eyes. Forty-nine per cent of the tumors developed during the first year of life. An hereditary factor could be established definitely in only two cases in this series. The authors suggest prophylactic irradiation of the apparently healthy eye in unilateral cases. This is harmless if given carefully and is of value for sterilizing groups of undifferentiated cells which are potential sites for the origin of new retinoblastomas. In their opinion the addition of chemotherapy, nitrogen mustard or triethylenemelamine to irradiation will improve the prognosis in advanced cases. Reese and his associates [253] obtained useful or limited vision in 36% of 148 patients with retinoblastoma treated with radiation. The greatest concern was late hemorrhage into the vitreous. They state that in the past 21 months they had treated 34 eyes with radiation and triethylenemelamine. The tumor seems to have been arrested, and good vision is present in 22 eyes (64%). The two agents seem to implement each other in a synergistic manner, and their combination offers the best method to date for treating this type of tumor.

Differential Diagnosis of Intraocular Tumors.—Fry and Spaeth [254] and Klien † discuss the clinical differentiating features of inflammatory and neoplastic lesions in the macular region. In discussing the possibility of diagnosing intraocular tumors by examining the subretinal fluid in cases of detachment of the retina, Christensen and Rowen [255] state that it is possible to identify tumor cells in the aspirated subretinal fluid but that "because of the technical difficulties involved and the obvious danger of extraocular extension of unrecognized tumors, this procedure is not recommended as a diagnostic aid." Andersen [256] notes that aspiration of subretinal fluid will be disappointing often because histologic evaluation of single cells or small clusters of cells is extremely difficult. Trephine biopsy following location of the lesion by an aspirating needle under ophthalmoscopic control is preferable. There is no definite proof that biopsy of a malignant melanoma involves the risk of spreading the tumor; nevertheless, biopsy should be reserved for cases in which diagnosis is not possible by other means.

† Klien, B. A., in discussion on article by Fry and Spaeth,[254] p. 354-355.

RETINAL DEGENERATIONS

Elwyn [257] discusses the clinical and pathologic characteristics of the heredodegenerations, which he classifies as those involving the elastic layer of Bruch's membrane, the neuroepithelium, the inner nuclear layer, and the ganglion cells. The heredoconstitutional defects involve the neuroepithelium and differ from the heredodegenerations in that they are not progressive. Manchester [258] presents a classification of the important hereditary eye diseases and the methods of determining the modes of inheritance. Newell and Koistinen [259] examined histologically five eyes from three cases of lipochondrodystrophy (gargoylism) and found evidence of degeneration of the ganglion cells and of the cells of the inner nuclear layer of the retina. This might explain the loss of vision in those cases in which it seems to be disproportionate to the density of the corneal cloudiness which is characteristic of this condition.

De Silva and Tennekoon [260] present two cases of amaurotic familial idiocy in Sinhalese children as further proof that this condition is not confined exclusively to Jewish children. Shapira and Leight [261] demonstrated fatty degeneration of the ganglion cells of the macular retina, marked loss of ganglion cells in the peripheral retina, and optic nerve atrophy in a case of amaurotic familial idiocy. Cases of juvenile amaurotic familial idiocy (Vogt-Stock-Spielmeyer disease) are reported by Nissen [262] and by Roveda and Iribarren.[263]

McFarland [264] studied the clinical and pathologic aspects of heredodegenerations of the macula, which he divides into three clinical types, characterized, respectively, by a flat, circumscribed circular lesion, by an elevated cystic lesion, which ruptures in adolescence or adulthood after formation of a pigment ring, and by a salt-and-pepper-like macular pigmentation. Mylius [265] presents three cases to demonstrate that the typical heredodegeneration of the macula is not confined always to the foveal region but may involve the periphery in juvenile, as well as in adult, cases. Friemann [266] reports the association in two brothers and a sister of juvenile macular degeneration and choreiform hypermotility. Both the eye and the nervous system disturbances were presumed to be hereditary. Davis and Hollenhorst [267] found bilateral symmetrical progressive macular degeneration of the pigment-stippling type in 24 persons belonging to the same family, which consisted of 148 members, in five generations. All the affected persons were almost completely color-blind. Landolt [268] observed foveal degeneration, reduction of central vision, and anomalous color perception in a brother and sister; only severe disturbance of color vision was present in another sister. On the basis of their studies of three families, Sorsby and Davey [269] describe, as a clinical entity, dominant macular dystrophy, a strictly localized central lesion, symmetrical in location and in extent in the two eyes, and ophthalmoscopically similar to the recessive macular dystrophy of the Stargardt type.

Sorsby and Davey [270] point out also that generalized choroidal sclerosis is inherited in a dominant manner. Sandvig [271] found 13 persons with central areolar choroidal atrophy in four successive generations of one family. He determined that the mode of inheritance was autosomal dominant. He thinks that the ophthalmoscopic picture suggests angiosclerosis rather than atrophy. Mylius and Stark [272] state that in patients with central retinal degeneration in whom other causative factors, such as trauma, heredity, and inflammation, can be excluded, there are as a rule a significant increase in the β-lipoproteins and a shift in the lipoprotein spectrum characteristic of progressive obliterating atherosclerosis.

Cases of Oguchi's disease are reported by Biegel [273] and Durix and Gallet.[274] From his studies of dark adaptation in Oguchi's disease, Iinuma [275] concludes that light adaptation induces a contraction and dark adaptation a dilatation, both direct and consensual, of the capillaries in the retina and choroid.

Retinitis Pigmentosa.—Haig and Saltzman [276] state that the foveal cones appear to be involved at all stages of retinitis pigmentosa and that foveal threshold measurements are a more sensitive index of the progression of the disease than are measurements of visual acuity. According to Weiner and Falls,[277] a female carrier of retinitis pigmentosa can be recognized by the presence of a "tapetal-like" retinal luster in the perifoveal area. Such a person will pass the disease to 50% of her male offspring, and 50% of her female offspring will be carriers. Crick [278] reports a case with a fundus picture resembling that described by Weiner and Falls, in which retinitis pigmentosa, typical except for the absence of hereditary occurrence, developed later. He thinks that this woman might be "potentially the mother of a family in which sex-linked intermediate retinitis pigmentosa may occur."

Hervouët, Baron, and Lenoir [279] conclude from their examination of four globes that retinitis pigmentosa is a degenerative process based on a disturbance of nutrition leading to progressive sclerosis of the nutrient vessels of the eye and that this sclerosis provokes secondarily the specific disorders of the retina.

Bruna,[280] Colombi,[281] Esente and Doni,[282] and Cambiaggi [283] report the association of retinitis pigmentosa with various congenital anomalies, especially keratoconus. It is interesting that all these reports appeared in Italian journals. Mathias [284] reports a case in which retinitis pigmentosa was associated with rheumatoid arthritis, bilateral scleromalacia perforans, and thrombosis of the left central retinal vein.

The Electroretinogram and the Electroencephalogram in Cases of Night Blindness.—Straub [285] states that the electroretinogram can be normal in cases of central tapetoretinal degeneration but that the b-wave is suppressed or absent in cases of disseminated tapetoretinal degeneration. According to Riggs,[286] the electroretinogram is practically absent in retinitis pigmentosa, even in cases with relatively slight impairment of vision. In congenital night blindness with normal fundi, the electrical responses are smaller than those of normal persons and require much more intense stimuli, but the form of the response is similar to that of normals, especially in the dark-adapted state. In cases of macular degeneration, the electroretinogram is practically normal, even when the defective macula only is stimulated by the test light. According to Bornschein and Vukovich,[287] there is reversible extinction of all the components of the electroretinogram in night blindness due to vitamin A deficiency, while only the b-wave is extinguished in congenital night blindness.

Dieterlé [288] thinks that the electroretinogram will differentiate, within certain limits, between primary and secondary pigmentary degenerations of the retina and is a justifiable method for clinical use. Armington and Schwab [289] state that the electroretinograms of congenital night blindness without fundus pathology seem to display only photopic components, whereas the response of the normal eye is complicated usually by the intrusion of scotopic potentials. The existence of clear-cut alterations is of pertinent significance when one is clinically evaluating alleged night blindness, especially in the military service, where the question of psychogenic complaints or malingering may be raised.

François, Stefens, and Derouck [290] state that the electroretinoencephalographic syndrome which they obtain by the simultaneous study of the electrical response of the retina and of the visual cortex to a light stimulus, either single or repeated, gives objective data which furnish an indication of the conduction time between the retina and the cortex and of the blocking effect of the retinal lesions. François, Stefens, and Derouck [291] and Streifler and Landau [292] call attention to the electroencephalographic abnormalities found in a rather high percentage of patients with retinitis pigmentosa.

Treatment of Retinitis Pigmentosa.—Fornaro [293] states that the effects of the treatment of retinitis pigmentosa with corticotropin and the melanophore hormone have been indeterminate as yet but that further trial is warranted. Payrau and Selve [294] report the results of treatment with intermedin, the melanophore pituitary hormone, in 21 cases of retinitis pigmentosa, two of essential day blindness, and two of albinism. They observed a favorable effect on the visual fields and night vision but no effect on the daytime visual acuity. Neither progression nor regression of the retinal lesions was observed ophthalmoscopically during a two- to three-year period. Leo and Lidman [295] report surprisingly good results from the treatment of retinitis pigmentosa with bishydroxycoumarin (Dicumarol). They state that all the patients have retained the degree of improvement initially reached, even though, in most cases, the drug has been discontinued for a long period of time. It would seem that further controlled investigations of these methods of treatment should be carried out.

Tapetoretinal Degeneration of Late Onset.—François and Decock ‡ describe two cases of nonfamilial tapetoretinal degeneration, which were characterized by a late onset, at 62 and 65 years of age, by rapid evolution, and by the lack of parallelism between the loss of peripheral vision, which was complete, and that of central vision, which was relatively well preserved. Scullica [296] states that 18% of his cases of retinitis pigmentosa started in adult life. When evaluated on the basis of heredity, onset, first manifestations, visual acuity, visual fields, light sense, and ophthalmoscopic appearance, it would seem probable, he thinks, that this adult form of pigmentary degeneration of the retina is an expression of meningoencephalitis and is independent of hereditary factors.

MACULAR LESIONS

Savin,[299] Evans,[300] and Davenport [301] discuss various phases of the significance of changes at the macula. De Gennaro [302] and Nirankari [303] describe the macular picture in cases of eclipse blindness. Bennett [304] discusses the relationship between central serous retinopathy and disciform degeneration of the macula. In his opinion the basic lesion in disciform degeneration of the macula is rupture of Bruch's membrane with transudation of plasma or blood from the choroid. Frayer [305] made a histologic study of 24 cases of elevated lesions at the macula. Thirteen of the eyes had been removed for malignant melanoma. Among other findings, there was evidence supporting the opinion that some cases of disciform degeneration result from the organization of spontaneous hemorrhage.

Kleinert [306] describes a primary folding of the central retina which he observed in six patients in the older age group. In the early stage there was no visual disturbance; later there was metamorphopsia, and still later, irreparable reduction of vision. In the later stages detachment of the posterior vitreous was demonstrated

‡ References 296-297.

in all cases. Kleinert thinks that these changes resulted from a localized circulatory disturbance in the smaller vessels.

TOXIC AND OTHER INJURIES OF THE RETINA

Lincoff [307] reports a case of loss of vision caused by quinine in which there was rapid improvement in central vision and gradual widening of the visual fields during a period of three and a half months. However, seven months later the residual field defects were found to have increased considerably. From observation of the ophthalmoscopically visible course of events in a case of quinine amaurosis, Drance [308] concludes that quinine has a direct toxic effect on the nerve cells of the retina and that vasoconstriction is a secondary feature. Electroretinographic studies by Vainio-Mattila and Zewi [309] and by Berggren and Rendahl [310] indicate that the primary damage occurs in the ganglion cells of the retina and that later the damage extends to the first and second neurons.

Studies on the visual toxicity of methanol in experimental animals by Praglin, Spurney, and Potts [311]; Gilger and Potts [312]; Potts,[313] and Potts, Praglin, Farkas, Orbison, and Chickering [314] indicated that formaldehyde is the proximal toxic agent in methanol poisoning; that eyeground changes are not seen in nonprimates, in which acidosis occurs rarely; that, despite treatment with base, most monkeys show retinal edema, which may extend to the disc, and that the only consistent early change in sections of retinas from methanol-poisoned, bicarbonate-treated monkeys is cyst formation in the external nuclear layer. In an animal which survived nine days, there were possible changes in the ganglion cells of the retina and demyelination of the optic nerve.

Kleinfeld and Tabershaw [315] report two cases of carbon disulfide poisoning; one patient had hemorrhages in each retina; the other had "crumb-like exudates" in the upper temporal quadrant of the right retina.

Doggart [316] notes that boxers may have various types of damage to the eyes, such as detachment of the retina, hemorrhage into the choroid, retina, or vitreous, rupture of the choroid, cystic and pigmentary changes at the macula, and optic atrophy from avulsion of the nerve or hemorrhage into the nerve sheath. In Löhlein's [317] opinion a boxer who has had a retinal detachment should be advised to give up boxing. While the reattached portion of the retina is less likely to become detached again, its fixation probably predisposes to detachment of the rest of the retina in response to further trauma. Bischler and Marty [318] warn of the possible misinterpretation of the post-traumatic chorioretinopathy of Siegrist type, which can assume the characteristics of a long-healed lesion within a week after the trauma. Dellaporta [319] reports a case in which, seven years after a contusion of the globe, there was marked hypotony with resultant papilledema, edema of the macula, and four small groups of radial folds around the macula as an expression of edema *ex vacuo*. Nano and Scenna [320] describe the development of unilateral traumatic retinal angiopathy in two cases within a few hours after blunt injury to the skull. Charamis [321] reports a case in which the passing of a bullet through the orbit without touching the globe produced the picture of closure of the central retinal artery. In three other cases in which a bullet penetrated the sclera, sealing of the associated retinal tears resulted in excellent vision.

Naunton and Forrester [322] observed hemorrhage into the vitreous of each eye of a premature infant, due seemingly to constriction of the neck during delivery because of an eclamptic convulsion after the head had been delivered. But the

hemorrhage increased markedly between the 9th and the 11th day and was still worse on the 30th day. However, it had largely cleared at seven months, and the retinas were normal except for a small myopic crescent in the right eye.

Byrnes, Brown, and Rose [323] and Byrnes, Brown, Rose, and Cibis [324] describe the clinical and histologic characteristics of the chorioretinal burns produced by atomic flash in experimental animals. The lesion produced is round and sharply circumscribed. When the burn is caused by a flash within eight miles, there is a deep central hole with or without hemorrhage, surrounded by a "halo" of dirty-gray color, and coagulation necrosis with major tissue and cell destruction is seen histologically. When the flash occurs at greater distances, the central hole is replaced by a yellowish-white plaque, and coagulation necrosis without major tissue and cell destruction is seen histologically. Landesberg [325] reports that a patient glanced over his left shoulder at an atomic flash. He was blinded for several minutes. The vision of the right eye cleared in about seven hours, but a central scotoma remained permanently in the left eye. Ophthalmoscopic examination three days after the incident revealed a large white "exudate" in the macular region with a hole at the site of the fovea and with some edema and one superficial hemorrhage in the surrounding retina. A pigmented area of about ¼ disc diameter was seen in the macula two years later.

Biegel [326] states that there is evidence that the retina undergoes degenerative changes with doses as low as 2000 r from the betatron. Minimal atrophy of the bacillary layer in the periphery of the retina was noted in rabbits after doses of 3000 to 4500 r. Cibis, Noell, and Eichel [327]; Brown, Cibis, and Pickering,[328] and Cibis and Brown [329] report on the effects of radiation on the eyes of experimental animals. They state that direct exposure of the monkey's eye to 10,000 r γ-radiation caused severe iridocyclitis, retinal edema, papilledema, punctate and flame-shaped hemorrhages in the retina, and, in some cases, severe hypotony. The most significant histologic change in the eye of adult mammals following high-intensity radiation is the death of the rod-cell population. Essentially the same effects were produced in the retina by x-radiation and by other kinds of ionizing radiation. Attention was called to the difference between acute radiation retinopathy and the late radiation retinopathy resulting from induced aplastic anemia and agranulocytosis, or abiotrophic conditions in which the retinal changes usually are of vascular origin and are located in the inner rather than in the outer layers of the retina.

OPTIC NERVE

Sengupta [330] describes the development in four cases of chronic simple glaucoma of new-formed veins establishing collateral circulation between the central vein and a large branch vein which was pressed on by a sclerosed artery. Hedges and Walsh [331] found at necropsy subhyaloid hemorrhages, hemorrhage into the vitreous, and massive hemorrhage invading the subdural and subarachnoid spaces of the optic nerve sheaths homolateral to the carotid artery into which 70% Diodrast had been injected for angiocardiography. Since there was no blood in the intracranial meningeal spaces, the hemorrhages into the optic nerve sheath were evidently an isolated phenomenon, due to intracranial venous stasis associated with a rapid rise in intracranial pressure.

Anatomy.—François, Neetens, and Collette [332] studied the anatomy of the vascular supply of the optic nerve by the technique of microarteriography. This study has been summarized previously by Payne.[333] Levine and Bronstein [334] present the

histologic findings in a case of foreign body granuloma of the sclera near the optic nerve sheath and in two cases of metastatic carcinoma of the optic nerve sheath as evidence that particulate matter can be transmitted from the cranial cavity via the optic nerve sheath.

Congenital Anomalies.—François and Haustrate [335] describe a coloboma of the iris, choroid, and optic nerve in a typical case of mandibular dysostosis. Perkins [336] observed bilateral generalized constriction of the fields and ring scotomas suggestive of hysteria, but constant on repeated examinations in a 20-year-old woman with deep, but not marginal, cupping of the optic discs, which was interpreted as representing an atypical coloboma. Caccamise [337] demonstrated relative bitemporal defects in the visual fields of a patient with moderate myopia, inferior conus, situs inversus of the disc, and lack of pigmentation in the choroid below and nasal to the disc.

Bedell and Jokl [338] describe the various types of epipapillary tissues which can arise from proximal rests of the hyaloid artery, from vestiges of the wall of the proximal part of Cloquet's canal, and from the remnants of the glial coat of the hyaloid artery. Planten [339] observed the occurrence of pseudopapilledema of rather peculiar type in all the members of a certain branch of a family. The elevation of the disc in some was sufficient to raise the suspicion of papilledema. On the basis of his study of four cases of unilateral pseudoneuritis or pseudo-choked-disc in myopic eyes, Badtke [340] concludes that this anomaly cannot be due to the presence of a too small scleral foramen but must be caused by a disturbance in the normal course of papillogenesis. Cristiansson, Haptén, and Krakau [341] describe a device which permits measurements of variations in elevation of the optic disc of as little as 0.1 D. This would be of value, in their opinion, in the differential diagnosis of papilledema, optic neuritis, and pseudopapilledema and in following the course of increased intracranial pressure.

Optic Neuritis.—In discussing the differential diagnosis of optic neuritis, Chamlin [342] states:

> In my experience, when a mass lesion is found compressing an optic nerve, the initial field defect is that of a peripheral defect corresponding to the mechanical pressure on the peripheral fibers. If increased, such peripheral defect will progress to involve a more and more central portion of the field until it finally reaches fixation. This should not be called a central scotoma but merely central involvement by central spread of a peripheral indentation.

Mancall [343] reports a case of opticociliary neuritis, the association of optic neuritis with internal ophthalmoplegia. The etiology was not determined. Bedrossian [344] observed a case of bilateral neuroretinitis following measles. Shechter, Lipsius, and Rasansky [345] observed unilateral retrobulbar neuritis as a late complication of infectious mononucleosis.

Nonnenmacher [346] reports a case of so-called lactation optic neuritis but advises caution in making such a diagnosis without repeated ocular and neurologic checks to exclude multiple sclerosis. Taub and Hollenhorst [347] observed four cases in which loss of vision was due apparently to individual idiosyncrasy to sulfonamides. Two of the patients had bilateral optic neuritis, one had unilateral optic neuritis, and the fourth had normal fundi. Spontaneous recovery occurred in the three cases which could be followed. Kazdan and Kennedy [348] compare the results of treatment of optic neuritis not due to demyelinating disease by intravenous corticotropin and by intravenous killed typhoid bacilli. They obtained improvement in about 50% of the cases treated by each method, but they gave no details as to the degree of improvement.

Oehninger, Rodriguez Barrios, and Gomez Haedo [349] state that the characteristics of optic neuritis caused by pentavalent arsenicals are marked narrowing of the visual fields, preservation of a reasonable degree of central visual acuity, and the absence of visible optic atrophy at the beginning of the process. They report two cases in which the visual disturbances developed after 17 and 14 days, respectively, of acetarsone (Stovarsol) therapy. In both, the visual fields improved under treatment with dimercaprol U. S. P. (BAL), but only after a delay of about two months.

Carroll and de Roetth [350] state that within a few minutes after the retrobulbar injection of procaine there was a partial or complete block of the extraocular muscles and a partial or complete block of the orbital sensory nerves, including the optic nerve, with varying reduction of vision, even to the point of complete blindness. The vision returned to normal within one-half to two hours in all their cases, and there were no permanent residuals.

Janssen and Böke [351] note that, when edematous swelling and elevation of the optic discs occur in the course of tuberculous meningitis, it is often impossible to differentiate between choked disc and optic neuritis, because tests of function cannot be made. Most of these lesions have gone on to optic atrophy. They seem to have increased in frequency since the introduction of isoniazid in the combined therapy.

Prater and Lam [352] found bilateral edema and elevation of the optic discs in a youth of 17 years who had acute loss of vision in the lower field of the right eye. The papilledema receded in about two weeks and was thought to have been secondary to serous meningitis. The inferior altitudinal anopsia persisted and was explained on the basis of spastic or embolic closure of the superior branch of the central retinal artery, since there was residual pallor of the upper temporal quadrant of the disc. Blood cultures were negative.

Optic Atrophy.—In a child, aged 4 years, Carreras [353] observed bilateral incomplete optic atrophy, which was attributed to the anoxemia that resulted from severe prepartum hemorrhage in the mother. Carreras discusses the characteristics of this type of optic atrophy, which, he says, is always incomplete and not progressive. There is a tendency to improvement in vision during the early years of life. King and Passmore [354] studied the features of nutritional amblyopia in 22 prisoners of war. The visual loss started on the average about 11 months after the beginning of deprivation of food. Night blindness was less prevalent in the men with amblyopia than in other prisoners of war. Electroretinograms suggested that one site of pathology is in the rods and cones of the retina and that optic atrophy, when present, is of ascending type. Šuster [355] and Zlámal [356] report that penicillin is ineffective in the treatment of tabetic optic atrophy.

Tumors of the Optic Nerve.—Oribe, Zimman, and Franke [357] report the clinical features and pathologic findings in three cases of glioma of the intraorbital portion of the optic nerve. Hummelt [358] observed remarkable preservation of vision and visual fields in the left eye of a 6-year-old boy with exophthalmos and a choked disc of 3 to 4 D., in whom a spongioblastoma was found to involve the optic nerve from the globe to the optic foramen. In the author's opinion a primary transcranial approach is preferable for the removal of a tumor of this type. Craig and Dodge [359] report that there was no evidence of recurrence of the tumor in a 14-year-old girl who had had a fibrous astrocytoma of the orbital portion of the optic nerve removed transcranially eight years before. Love, Dodge, and Bair [360] state that the prognosis is much more favorable in cases of low-grade astrocytomas located entirely within the orbital portion of the optic nerve or involving the intracranial portion of the nerve only

prechiasmally than in cases in which similar tumors involve the chiasm and optic nerves. The former can be removed completely by the transcranial route. One of the authors' patients was in good health 9 years, and another 12 years, after removal of the tumor.

In a 5-year-old girl with neurofibromatosis, Berg [361] found a glioma of the left optic nerve which had penetrated the sheaths of the nerve and spread into the orbit. Donahue [362] reports a case in which the left eye and a portion of the optic nerve had been removed at the age of 3 years because of the presence of a glioma of the optic nerve. An exenteration of the orbit had been done 15 months later. Almost 21 years later, the patient returned with a huge recurrence in the orbit but was otherwise well.

In a patient with moderate exophthalmos and moderate peripapillary edema but without much loss of vision, Chinaglia [363] found a primary alveolar meningioma of the sheath of the optic nerve. In a 26-year-old woman, Wallner and Moorman [364] observed a reddish-purplish mass covering the nasal half of the optic disc. It was elevated 4 D., was highly vascular, and was composed of numerous small round masses, so that it resembled a raspberry or cluster of grapes. The vision was normal. The tumor was thought to be a cavernous hemangioma of the optic disc. It showed no progression during a period of one and a half years. There were a number of similar lesions in the skin of the trunk.

McPherson [365] calls attention to the fact that hyaline bodies in the optic disc may simulate papilledema and may cause bizarre field defects. One patient in whom he observed hyaline bodies had no symptoms; another had only ocular complaints. The third patient had subjective neurologic symptoms but no objective neurologic findings, and a pneumoencephalogram and a ventriculogram were normal. McPherson thinks that this last case may be one of subclinical tuberous sclerosis.

In summarizing a review of the literature on tumors of the optic papilla, Wagener [366] notes that tumors of various types may arise primarily in the tissues of the papilla or may invade the papilla from the optic nerve proper or from the peripapillary retina or choroid. It has not been proved definitely that a malignant melanoma can develop primarily in the optic papilla.

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COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Edmund B. Spaeth, M.D., Chairman
William E. Krewson, 3rd, M.D., Clerk
Regular Meeting, Dec. 15, 1955

Excision of a Localized Iris Tumor Under Direct Vision. Dr. Wilfred E. Fry.

The following case was presented and the operative procedure described:

An elevated, pigmented lesion was observed in the lower nasal angle of the left eye. This measured approximately 2×3 mm. and appeared by ordinary observation to extend into the angle. The pupil was round, showed no evidence of distortion, and reacted normally. The lens, vitreous, and other structures of the eye were entirely normal. There was no evidence of pressure on the periphery of the lens with a dilated pupil.

The following operative procedure was carried out: A fornix-based conjunctival flap was made, extending from 4 to 10 o'clock. An incision was made through the sclera approximately 2 mm. behind the visible limbus and was carried straight down through the sclera by means of a Bard-Parker knife. The eye was penetrated by the knife at one point, and the incision was enlarged by scissors. A suture was placed on the corneal side of the incision, and by means of this the cornea could be raised. The iris could be inspected under direct vision. By means of an iris forceps, the iris was picked up at one side of the tumor, and a radial incision was made; the iris was stripped from the ciliary body to a point on the opposite side beyond the tumor, and a second radial incision was made. The incision was closed by two nonabsorbable (silk) surgical sutures and the conjunctival flap replaced. There were no complications, and postoperative recovery was good.

The pathologic diagnosis of the tumor was malignant melanoma.

DISCUSSION

Dr. E. W. Conway: I recall this case distinctly because the results of the P^{32} test were very interesting. As you recall, the first uptake of P^{32} was recorded as 11% in 24 hours, and the second uptake was reported as 22%. According to the criteria of Eisenberg, if the first-hour uptake of any suspected malignant lesion, or any lesion in the eye is less than 30%, the lesion is to be considered nonmalignant. However, if the count is more than 30% in the first hour for any suspected lesion, then the 24-hour count is indicated. If the 30% count rises to a higher one, the lesion is to be considered malignant. If, however, the count falls from the original figure, the lesion is usually considered to be inflammatory in nature.

The clinical appearance of this growth, at the time when the P^{32} test was performed, prompted us to do a 24-hour count, despite the fact that the initial first-hour count was only 11%. To my chagrin, I found that the count had risen to 48%. I should like to have reported this test as positive for a malignant lesion; however, after consultation with Dr. Eisenberg, it was felt it would be best to retain the criteria which were outlined formally in the paper.

Two conclusions may be drawn. First, iris lesions may not be so malignant when they are located solely in the iris, do not involve the choroid or ciliary body, and tend to show a low metabolic turnover of P^{32}. Second, as Dr. Fry suggested, the criteria for the evaluation of the P^{32} test for iris lesions must be revised.

Itching of the Eyes: An Inquiry into Its Causes. Dr. Thomas H. Cowan.

The physiologic principles of itching in general and their application to specialized ocular areas were first considered. A clinical experiment was described in which itch-provoking stimuli were applied to various parts of the ocular region

in an attempt to ascertain where and how itching was most easily aroused so that the source of pathological itching might be indicated. The causes of some clinical cases of itching were described. The results may be summarized as follows:

1. The theories of itching in general can be applied to the eye with reservations. The cornea, supplied with pain fibers only, does not constitute a source of itching according to the techniques used. The limbus and bulbar conjunctiva can be induced to itch only with difficulty, and when highly sensitized by a pathological condition of allergy.

2. The conjunctiva of the lids definitely responds to stimulation with itching, thus giving a clear-cut example of the ability of mucous membrane to itch.

3. The skin of the lids responds to stimuli in the same way as does the skin elsewhere.

4. The area of the lid margins, together with the cilia, respond to itch-provoking stimuli more readily than do other parts. Some obscure causes of pathological ocular itching originate here.

5. Stimulation of the itch-sensitized areas around the eyes reproduces the clinical symptoms, and removal of the sensitizing and irritating agent causes cessation of itching.

News and Comment

ANNOUNCEMENTS

Course in Slit-Lamp Biomicroscopy and Ocular Surgery.—The Committee on Postgraduate Education of the Montefiore Hospital announces an advanced course in Slit-Lamp Biomicroscopy of the Living Eye, combined with additional courses in Ocular Gonioscopy, Indirect Ophthalmoscopy, Surgery of Intraocular Foreign Bodies, Surgery of Cataract, and Glaucoma Surgery, to be given by the Montefiore Department of Ophthalmology, under the direction of Dr. Harvey E. Thorpe and associates. These courses will be given at the Montefiore Hospital, Pittsburgh, for five days, May 7 to 11, 1956, inclusive, from 8:30 a. m. to 4:00 p. m.

The fee for the course is $80.00. A deposit of $25.00 is required for registration.

For further information write to A. Lenas, Secretary of Postgraduate Ophthalmic Courses, 323 Jenkins Building, Pittsburgh 22.

Guest speakers: Dr. Robert J. Masters, Indianapolis, and Mr. Lee Allen, Iowa City.

Course in Histopathology of the Eye.—Dr. Gerald B. Kara, Ophthalmic Pathologist to the State University of New York College of Medicine at New York City, Brooklyn, will give a course in histopathology of the eye, June 4-9, 1956. For details, contact Mrs. Jackson, IN 2-4000, Ext. 343, or write % Department of Ophthalmology, State University of New York College of Medicine at New York City, 451 Clarkson Ave., Brooklyn 3.

The American Orthoptic Council Examination for Technicians.—The annual examination of orthoptic technicians by the American Orthoptic Council will be conducted in August and October, 1956.

The written examination will be nonassembled and will take place on Thursday, Aug. 23, in certain designated cities and will be proctored by assigned ophthalmologists.

The oral and practical examinations will be held on Saturday, Oct. 13, in Chicago, just preceding the meeting of the American Academy of Ophthalmology and Otolaryngology.

Application for examination will be received by the office of the Chairman of Examinations, Dr. Frank D. Costenbader, 1605 22d St., N.W., Washington 8, D. C., and must be accompanied by the examination fee of $30.

Applications will not be accepted after July 1, 1956.

Books

Glaucoma: Reports of a Symposium Organized by the Council for International Organizations of Medical Sciences. Edited by Sir Stewart Duke-Elder. Price, $7.50. Pp. 380, including index, appendices, and bibliography. Charles C Thomas, Publisher, 301 E. Lawrence Ave., Springfield, Ill., 1955.

The Council for International Organization of Medical Sciences periodically organizes symposia on various medical subjects. The meeting of the XVIIth International Congress of Ophthalmology, opening in Montreal, offered an excellent opportunity for the Council to organize a symposium on glaucoma, and accordingly a number of the foremost contributors to this subject, including anatomists, physiologists, pathologists, and clinicians were invited to meet in the Alpine Inn at St. Marguerite, in the Laurentian Mountains of Canada, ahead of the official opening of the Congress, in September, 1954.

This book, which consists of their deliberations, forms one of the most valuable contributions to our knowledge of glaucoma which has appeared within the last few years, consisting, as it does, of papers by experts in the field together with a frank discussion by their peers. Regardless of whether there emerged any unity of opinion—and, surprising to say, there seemed to be far more agreement than disagreement when the symposium closed—the presentation of the material from different points of view was valuable not only for bringing us up-to-date as to where we stand at present in glaucoma but for pointing the way for future research.

First things come first, and it was necessary for the symposium to agree on terminology. The final vote was to use the terms "closed-angle glaucoma" and "simple glaucoma" for the two different disease entities which have hitherto always been included under varying terms as one entity. Narrow-angle and wide-angle, acute or congestive glaucoma were, at least for the time being and the purposes of this book, put on the shelf. The fundamental problem of closed-angle glaucoma was to decide whether either of the extreme views which are commonly held is correct; namely, that closed-angle glaucoma is determined primarily and entirely by mechanical events in the angle of the anterior chamber, and that the initial cause is not the mechanical changes in the angle, but something that lies deeper, such as a vasomotor instability. This, to quote Duke-Elder, "leads to a localized rise in the pressure of the small blood vessels of the anterior segment of the uveal tract, so that an excess of fluid is poured out into the posterior chamber and anterior vitreous; in certain circumstances this may lead to widespread congestion and edema of the ciliary body. In an eye in which the drainage channels are free and the angle is wide, nothing untoward happens; the safety valve provided by the canal of Schlemm is effective. But in an eye in which the angle is narrow, the bellying forward of the iris causes a mechanical blockage we have already described. The occurrence, therefore, of an acute attack of tension in this view, although not caused primarily by the anatomical configuration of the angle, can be realized only if the angle is sufficiently narrow." Duke-Elder pointed out that if the mechanical view alone is correct, it is necessary to explain why every person with narrow angles does not get glaucoma. Why does it occur particularly in persons of an excitable temperament with vasomotor instability and under conditions of strain or excitement? Why does the pupil behave in this peculiar way only in people of this habit? And, finally, why, "after the disease has progressed for some time, but while the angle is still normally open, it often closes periodically in a regular rhythm, for example, every morning or every evening, without regard to light or darkness or movement of the pupil."

In simple glaucoma the two schools of thought are not nearly as widely separated as they are in closed-angle glaucoma. There are those who feel that simple glaucoma is primarily due to some impediment in the drainage of aqueous humor

in the trabeculae or in the drainage channels distal to Schlemm's canal, while there are others who think that the ultimate cause of the condition is more fundamental, and is, again, essentially a vascular disturbance. Duke-Elder suggests that any definition of simple glaucoma must include the fact not only that it is a disease wherein the ocular tension is raised, but also "a condition wherein the diurnal phasic variation of the eye is greater than 5 mm. Hg as measured on the Schiøtz tonometer, even though this variation constantly lies within normal limits."

One of the outstanding features of the symposium was the demonstration by Ashton of the anatomical make-up of Schlemm's canal and its drainage channels. Of the seventeen to thirty-five outlets from the canal which occur in man, Ashton does not believe that narrowing or obliteration could likely be a factor in the pathogenesis of glaucoma. However, the deep scleral plexus, containing large varicose vessels which receive aqueous from the relatively few outlets of the canal, is a likely place for any interference to cause a rise in pressure. The deep scleral plexus travels to the episcleral vessels through either direct or indirect anastomotic branches or passes downward in the sclera to pour into the emerging anterior ciliary veins. Ashton concludes that in passing out of Schlemm's canal the aqueous flows into a venous bed which is freely connected to both the internal ocular venous system and the external ocular venous system, and any interference at this site could cause a damming back of aqueous and an obstruction to outflow. Ashton insists that aqueous veins are not specialized structures in any sense other than being episcleral veins which contain a mixture of aqueous and blood in various proportions. All of the episcleral veins are potential conductors of aqueous. No afferent arteriolar connections could be found between Schlemm's canal and the arterial supply in this region. This is contrary to Friedenwald's earlier hypothesis.

It was generally conceded by the symposium that the normal intraocular pressure was lower than has generally been thought, and is probably more nearly that found by Goldmann with his new applanation tonometer, i. e., around 14.5 mm. Hg. According to him, pressures higher than 20 mm. Hg with this method are abnormal.

The chapters on the nature and origin of aqueous humor by Langham and Kinsey make for hard reading, and as far as clinical ophthalmology is concerned it can be said that our knowledge in this field has not yet reached the point where it can have practical application. The battle is still being fought, and there is still too much smoke to see much of what is going on. Langham seems to agree that the excess of osmotic pressure in aqueous humor over that in the blood is due to the secretion of ascorbic acid and the production of lactate and bicarbonate within the eye. He is not so sure that there is any active transport of cations, such as sodium, across the blood-aqueous barrier. He ends up with the conclusion that, with the exception of ascorbate, the transfer of solutes can be explained by the physical characteristics of the compound and the diffusion gradients acting across the barrier. Kinsey, on the other hand, still believes that sodium enters the posterior chamber by secretion, and that other substances, such as thiocyanate, enter by diffusion. Even the discussion which followed the presentation of this portion of the symposium kept pretty far away from the battlefield itself. Barany described the series of experiments in which, by eliminating the lens in rabbits, he combines the anterior and the posterior chamber into one.

The resistance to the outflow of aqueous humor was discussed by Barany, Goldmann, and Grant, the clinical aspects, and particularly the phasic variations, being discussed by Duke-Elder. There seems to be general agreement that the facility of outflow is subnormal in simple glaucoma, and continues to be subnormal even at times when the intraocular pressure itself is normal. On the other hand, in closed-angle glaucoma the facility of outflow is markedly decreased at the time of pressure elevation, but the net rate of flow does not appear to be characteristically altered. Duke-Elder calls particular attention to the diurnal phasic variations in the ocular pressure, which are increased in simple glaucoma. He believes that they can best be explained by a vascular origin, due to some diurnal variation of sympatheticotonia under the control of a center in the hypothalamic region. He

considers this rhythmic variation similar to other rhythms occuring in nature, such as sleep, bodily temperature, diuresis, etc., all of which have a neurohormonal control. The marked accentuation of these normal phasic variations in simple glaucoma, he believes, is due to a neurovascular instability, so that the nervous control which keeps the variations within well-defined limits in the normal eye becomes ineffective in the glaucomatous eye, and the changes in tension become magnified. He believes that the rising phase of tension in these phasic variations are due to a venous capillary constriction determined by a condition of sympatheticotonia, and the fall in tension due to vasodilatation, by a relaxation of the activity of the sympathetic system. In simple glaucoma, there are, therefore, two elements which obstruct the drainage of the aqueous: First is an organic obstruction, which can be measured by tonography permanently, and, added to this, a pressure on the intraocular capillaries varying with the state of sympatheticotonia. The drainage of the aqueous is either obstructed or facilitated by the venous capillary constriction or dilatation.

The discussion of gonioscopy was preceded by a paper by François. Provocative tests were discussed by Leydhecker, Kronfeld, and Duke-Elder. Weekers discussed the mode of action of medical and surgical methods of reducing ocular tension, and various clinical aspects of glaucoma were introduced by Hodgson.

After each section, the general discussion is recorded. It is to be hoped that a similar symposium will be held prior to the next International Congress and that by that time some of the questions which could not now be resolved will have been answered.

Zeitfragen der Augenheilkunde. By W. Hoffman and H. Gasteiger. Price, 36 D. M. Pp. 474, including index. VEB Georg Thieme, Hainstrasse 17/19 Aufg. C., Leipzig C.1., 1955.

Under the title "Timely Questions in Ophthalmology," the authors have collected a series of manuscripts presented at a graduate course in ophthalmology during the week of Aug. 4 to 9, 1952, in Berlin. The various problems discussed cover the entire field of ophthalmology. For those who read German fluently this volume will contain much of interest.

Atlas der Spaltlampengonioskopie. By Ernst G. A. van Beuningen. Price, 59 D. M. Pp. 142, with 141 illustrations, many in color. VEB Georg Thieme, Hainstrasse 17/19 Aufg. C, Leipzig C.1., 1955.

This "Atlas" represents the first serious attempt to document the findings of gonioscopy with those obtained by the use of a slit beam and high magnification. By using a contact glass with a slit illumination and high magnification, the author has investigated the normal angle and the pathology which is found there in various conditions, both preoperatively and postoperatively. For those who read German fluently, this book will be an extremely valuable adjunct to the library. It is hoped that eventually an English translation will be made for those less skilled in reading a foreign language. The illustrations are excellent, and the whole text is comparable to that of Vogt's atlas on slit lamp microscopy.

Brain Mechanisms in Diachrome. By Wendell J. S. Krieg. Price, $7.00. Pp. 188, with 55 illustrations. Brain Books, Box #9, Evanston, Ill., 1955.

There is a certain fascination about books on brain anatomy. A large part of this is undoubtedly due to the pictorial representation of the enormously complex cytoarchitecture of the brain. The presentation, visually, of pathways leading from cells in the cortex to their final destination in the muscles or sense organs is always spellbinding, perhaps because most of us have visual memories. This fascination is doubly intensified when the material to be presented can be depicted in three dimensions. Dr. Krieg has been the pioneer in the use of this method in neuroanatomy. His previous book, entitled "Functional Neuroanatomy," was published in the second edition in 1953 and employed unique techniques in the presentation of the illustrations in three-dimensional form. This book is a continuation and an extension of

these methods. With the use of transparencies in color "the diachrome reconstructions consist of six double sheets—twelve pages—the two sides of each depicting one group of structures as seen from the medial and lateral views."

The first forty pages are devoted to an elementary discussion of the building blocks of the nervous system, the comparative embryology of brains in different animals up to and including man. The rest of the book treats of brain anatomy from the point of view of function. The section on vision, unfortunately, is quite limited, but excellent. The illustrations are without doubt the most beautiful that have ever been drawn to depict brain anatomy. All of the illustrations were made by the author, whose abilities in medical illustrating rank him among the best. Many of the illustration are in the style of, and are quite equal to, the best of Max Brodel. In others he has perfected unique and original techniques. No one could pick up this book to look at it without buying it. As a source of training for residents and those reviewing for examinations in brain anatomy it is unsurpassed.

Transactions of the Pacific Coast Oto-Ophthalmological Society. Vol. XXXVI. 1955.

The 39th Annual Meeting of the Pacific Coast Oto-Ophthalmological Society was held in Portland, Ore., from Monday, May 16, to Thursday May 19, inclusive. The list of ophthalmological papers presented is as follows:

President's Address: Some Products of Twenty Years' Experience with a Physiologic Hypothesis of Allergy — L. Weston Oaks, M.D.
Recent Advances in Ocular Pharmacology — Irving H. Leopold, M.D.
Malignant Melanoma of the Iris at Age 15: A Clinicopathologic Study — Alan J. Rosenberg, M.D.
Change-Overs from Eso- to Exotropia — Roderick O'Connor, M.D.
Differential Diagnosis of Dark Lesions of the Posterior Fundus — J. W. Bettman, M.D., and Victor Fellows, M.D.
Glaucoma Survey of 1000 Hospital Patients — Daniel G. Vaughan Jr., M.D.; Taylor Asbury, M.D.; William F. Hoyt, M.D.; Rudolf H. Bock, M.D., and Jean M. Swain, M.D.
Epithelial Invasion of the Anterior Chamber — A. Edward Maumenee, M.D., and C. Richard Shannon, M.D.
Temporal Arteritis — A. Ray Irvine Jr., M.D.
Optochiasmic Arachnoiditis — Richard Sonntag, M.D.
Radiographic Interpretation in Ophthalmology — William R. Nelson, M.D., and Elmer Ng, M.D.
Diagnosis of Malignant Melanomy by Subretinal Fluid Studies — Leonard Christensen, M.D., and Gerald E. Rowen, M.D.
Clinical Tears in the Retina without Detachment — Bayard H. Colyear, M.D., and Dohrmann K. Pischel, M.D.
Symposium — Drs. Leopold, Swan, Kimura, and Hogan

Indian Yearbook of Ophthalmology. Edited by Vaman D. Sathaye. Price not given. Pp. 194, including index, with a supplement of a list of eye specialists in India. 502 Narayan Peth, Poona 2, India, 1954.

This is a selected review of abstracts published in the English language covering ophthalmic literature for 1954. It also includes proceedings of various Indian ophthalmological societies. A few original articles have also been included. This volume will naturally be of chief interest to ophthalmologists practicing in India.

L'Annéethérapeutique en ophtalmologie. G. W. Jayle and A. Dubois-Poulsen. Vol. 5. Pp. 523, including index. Librairie Fueri-Lamy, 21, Rue Paradis, Marseilles, 1954.

This is a series of manuscripts in French on a number of unrelated ophthalmological subjects. The first 174 pages are devoted to the eye and the general circulation. The rest of the book covers the field of general ophthalmology, with emphasis on treatment.

Eye and Midbrain (Auge und Zwischenhirn). Prof. Dr. Rudolph Thiel, Editor. Price, 19.60 Dm. Pp. 209, with 125 partly colored illustrations. Ferdinand Enke, Hasenbersteige 3, Stuttgart, W., 1955.

This book reports on recent examinations of the correlations between eye and midbrain.

Becker reports upon discovery of a nuclear area of the sympathetic nervous system in the third neuron of the retina and its proved and still hypothetic actions. A chapter is added on the topochemistry of the retinal layers (Eichner). Rohen and Mrodzinsky record the structural changes of the nuclei of the retinal nerve cells due to light stimuli. Frey describes the exact course of the pathway of autonomous nerve fibers from the eye to the recessus opticus of the diencephalon and reports on its phylogenetic correlations.

The influence of light on the metabolism of the body by means of the eye is treated by Hollwich. After the report of numerous experiments on animals the influence of light on the pathophysiology of man is demonstrated. The author comes to the conclusion that there are steering influences from the eye via midbrain to the pituitary gland due to light.

Leopold-Messner found that in persons with glaucomatous eyes regulation of body functions due to the autonomous nervous system is different from that in healthy people. He declares that a glaucomatous eye is a center of irritation of the autonomous nervous system.

On the basis of the preceding explanations, Thiel and Hollwich treat the question of afferent and efferent reflexes of regulation between the eye and the diencephalon, with particular consideration of the eye pressure. After enumerating the literature concerning this theme, they describe in detail the influence of functional tests, of psychical trauma, and of sedative drugs on eyes with primary glaucoma. On the basis of their statements, the authors come to the conclusion that any irritation of the reciprocal reflex mechanism of regulation between eye and midbrain can cause glaucoma.

It is obvious that this book is controversial in that it deals with subjects which have been talked about by many but accepted by few. It is doubtful whether this volume will change the skepticism which it seems necessary to maintain in dealing with the influence of the midbrain on the eye. There is considerable justification for many of the concepts which this volume delineates, but proof of these concepts has not as yet been offered, and in most instances the ideas are expanded beyond the evidence which supports them. It should be read by all those interested in the pathophysiology of glaucoma.

Experimental Tuberculosis: Bacillus and Host. Edited by G. E. W. Wolstenholme and Margaret Cameron, for The Ciba Foundation. Price, 42 s. J. & A. Churchill, Ltd., 104 Gloucester Pl., London W.1, 1955.

This book reports the Symposium on Experimental Tuberculosis by a group of leaders in this field. The value of these Ciba publications has already been pointed out in previous reviews. While this volume will not be of immediate interest to most ophthalmologists, those who are engaged in experimental work in tuberculosis of the eye will find it a most important publication.

The chairman of the Symposium was Dr. Arnold Rich, whose work was largely responsible for our current ideas of the difference between allergy and immunity in tuberculosis, and the effect of the allergic response on the clinical course of tuberculosis. It was due largely to his work that the Baltimore school started their experiments in desensitization. In addition to the section on tuberculosis, there is a small addendum on Experimental Leprosy, under the chairmanship of T. D'Arcy Hart.

Current Therapy. Edited by Howard F. Conn. Vols. 5-8. Price, $11.00 each. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5, 1956.

This eighth edition of the Annual Review of Current Therapy follows the previous editions in form and context. Only one ophthalmologist is a contributor to this volume, Dr. Max Fine. He writes of the treatment of neuritis, optic and retrobulbar, with the corticosteroids and fever therapy.

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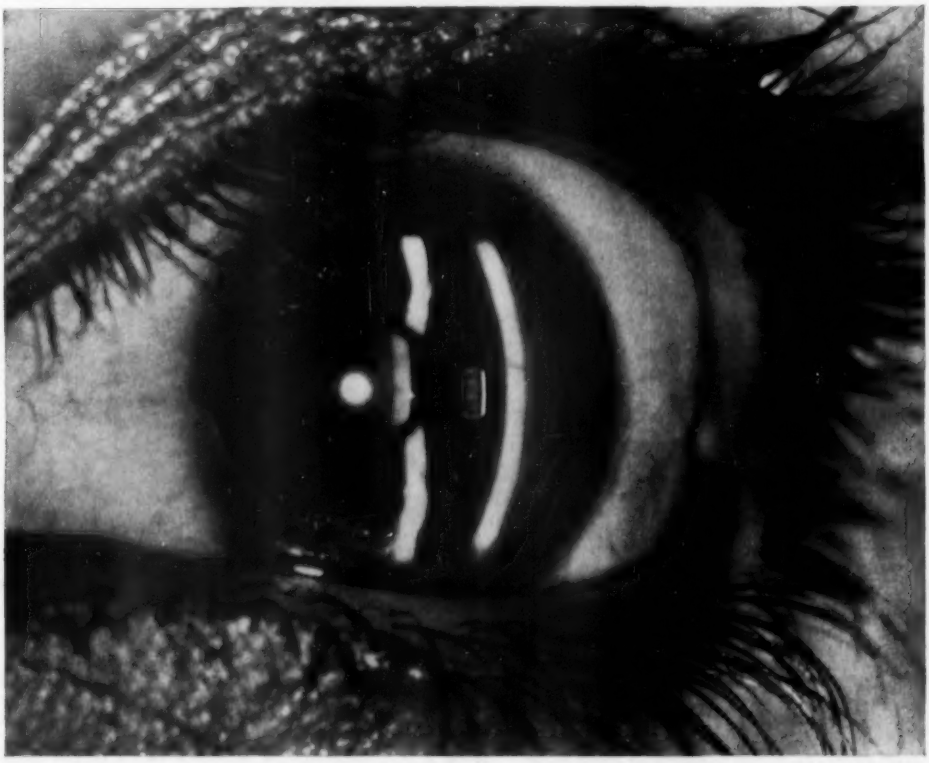

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Reference: 1. Hogan, M. J., Thygeson, P. and Kimuras, J., *Arch. Ophth.* **53**:165, Feb. 1955.

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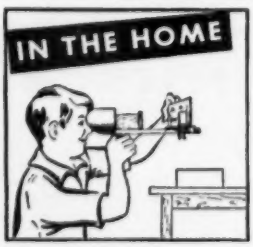

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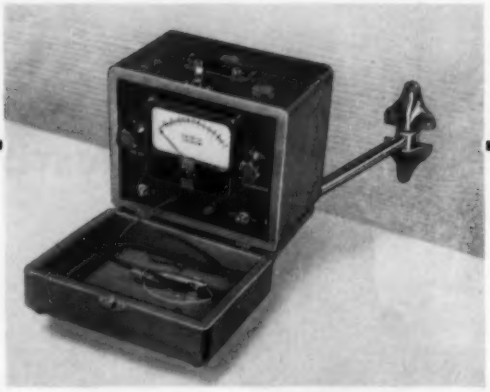

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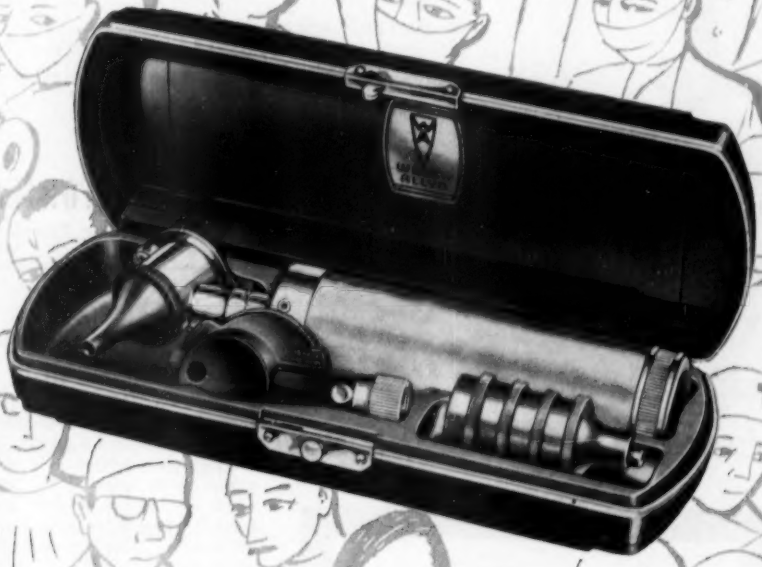

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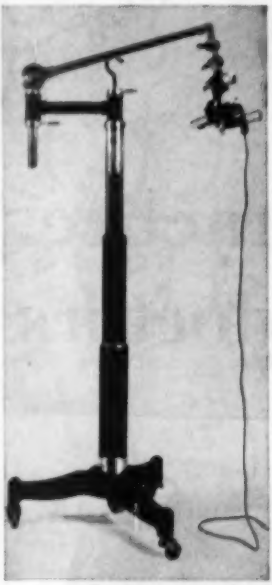

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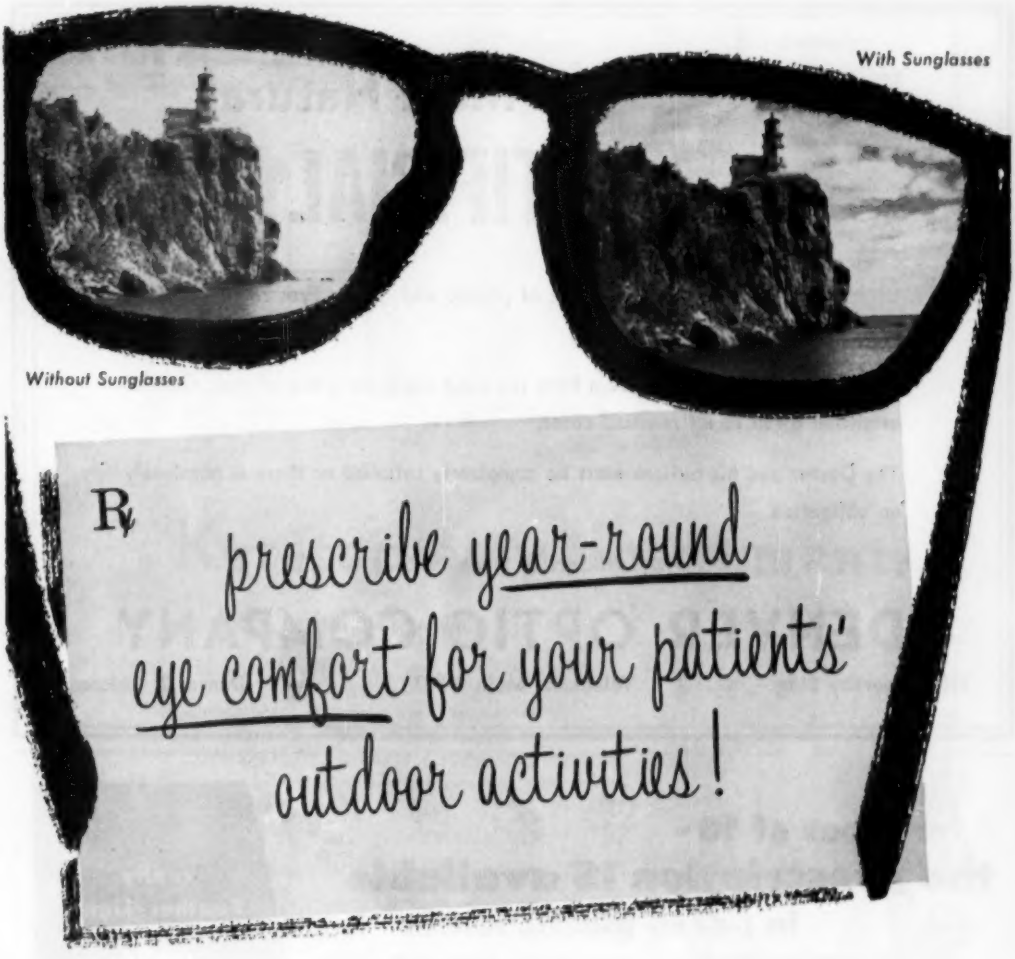

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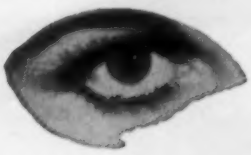

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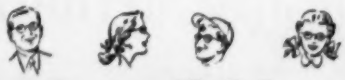

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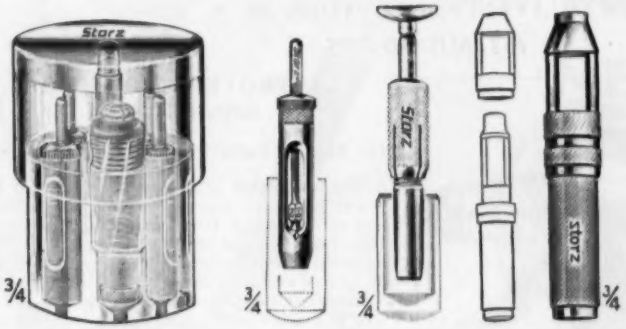

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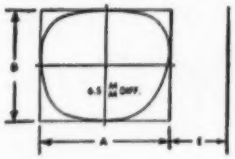

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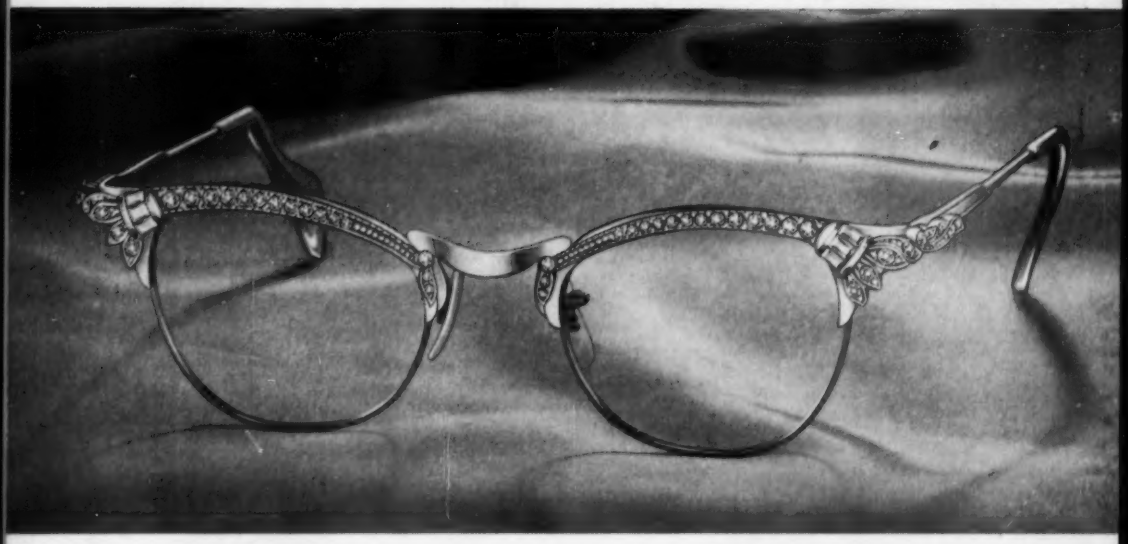

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